VOLUME 52 NUMBER 4 APRIL 1959

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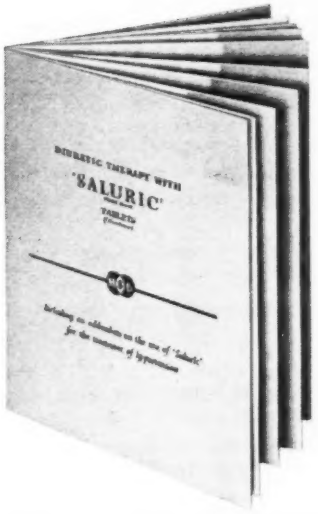

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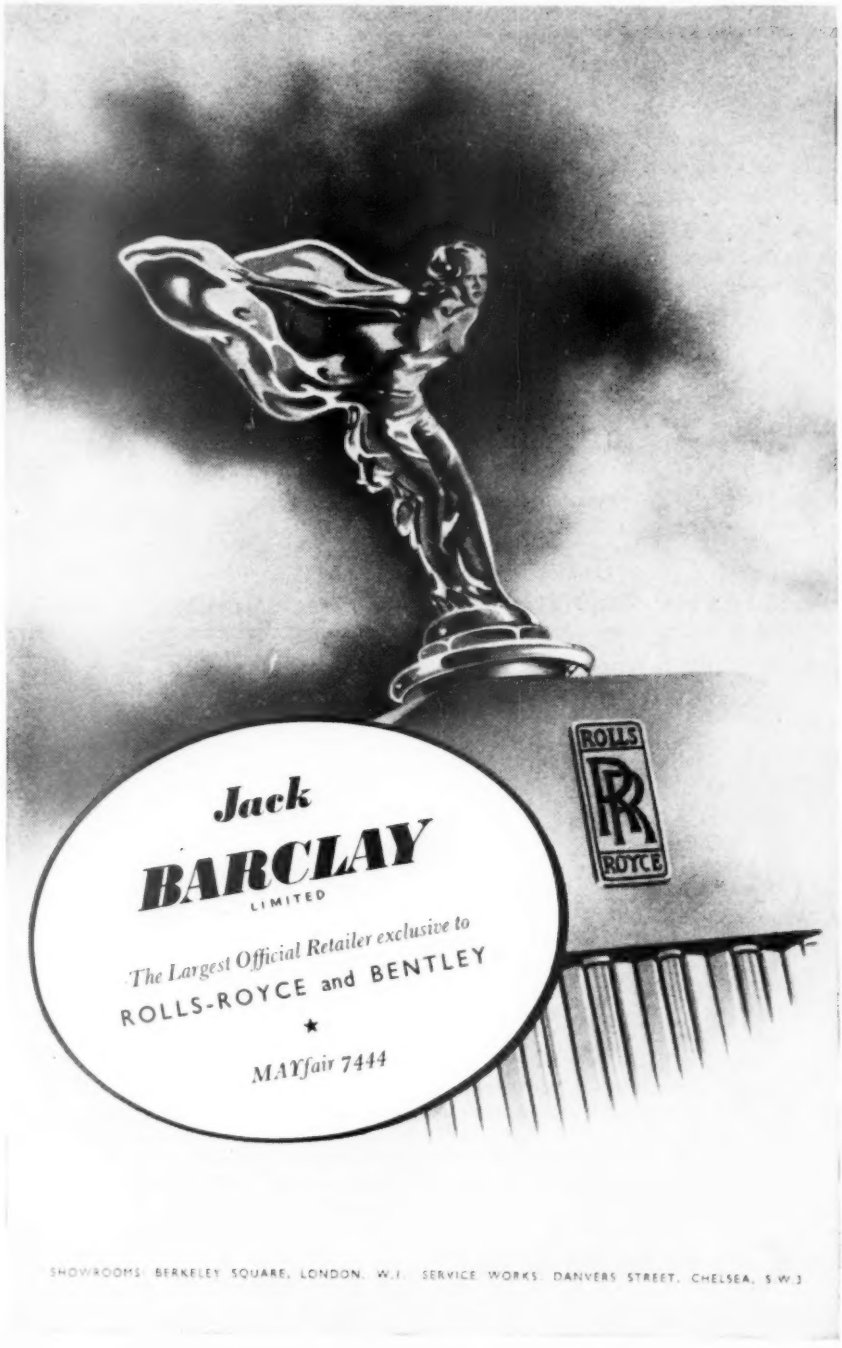
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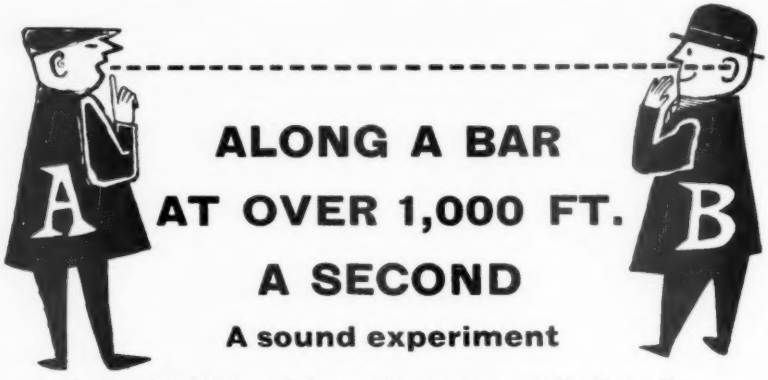

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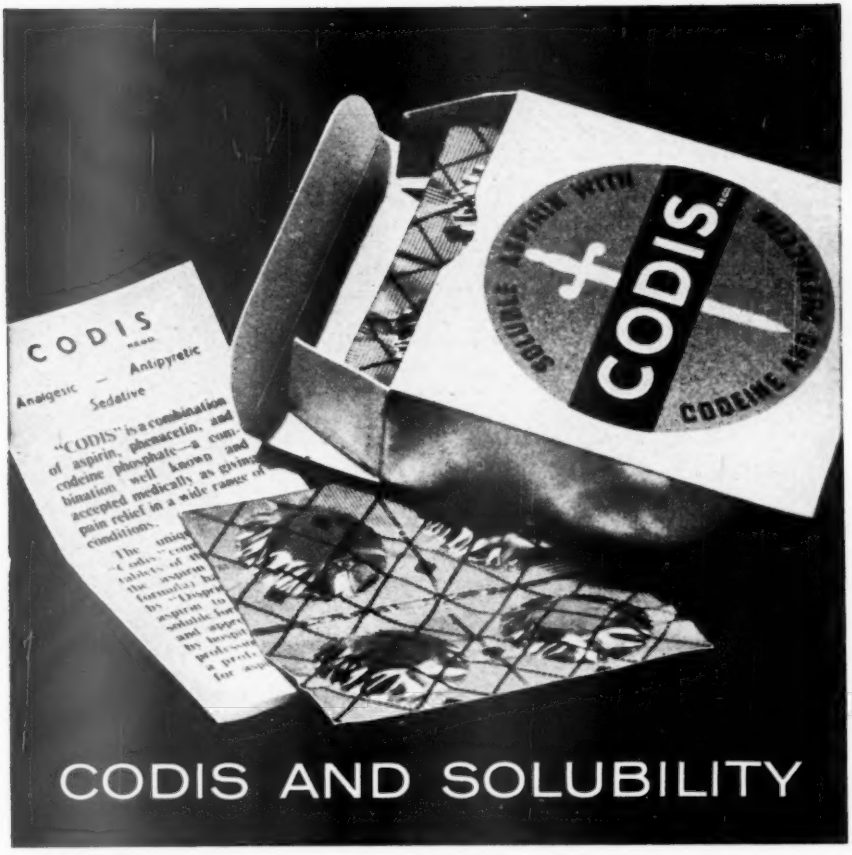
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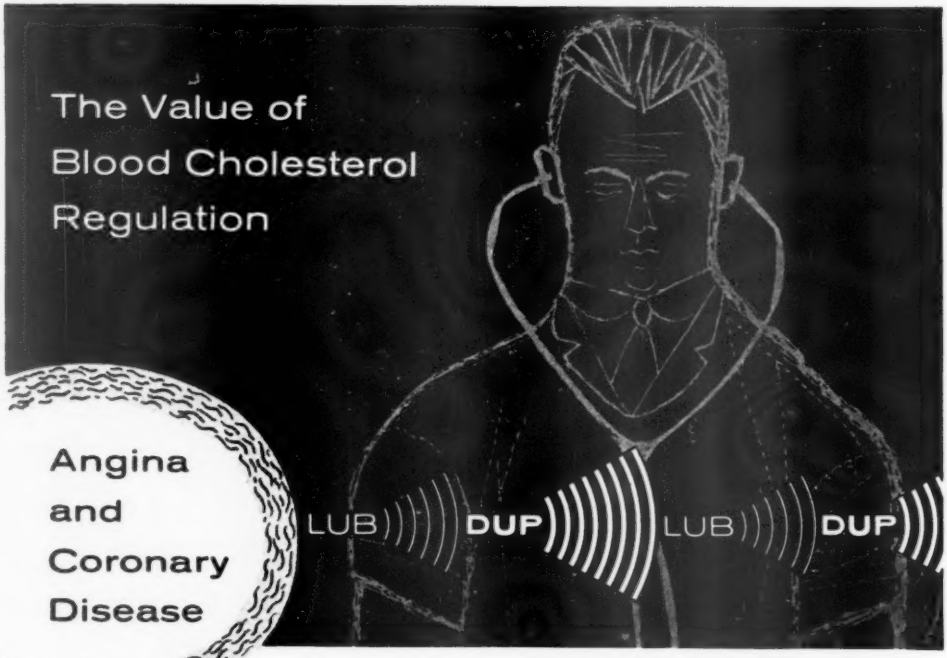

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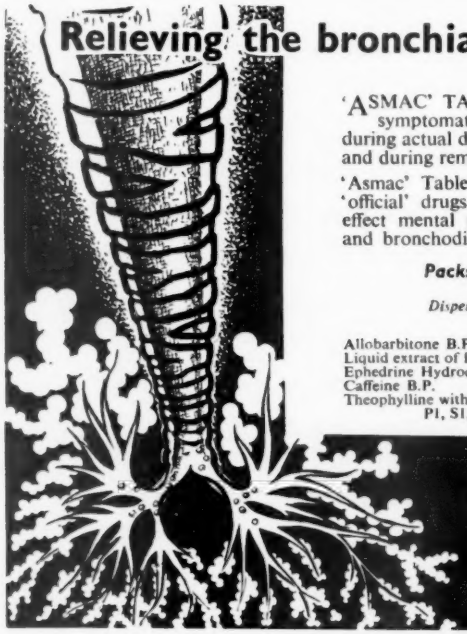

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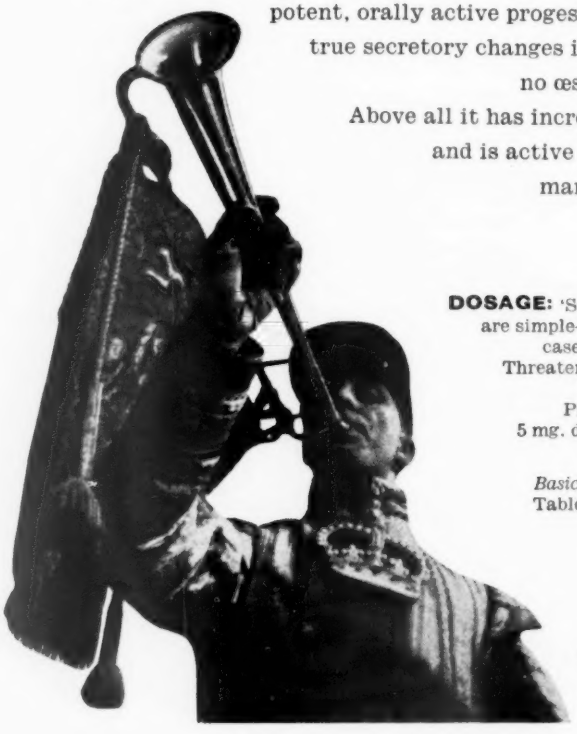

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President—DOUGLAS MACLEOD, F.R.C.O.G.

Meeting
October 24, 1958

Then and Now—A Tribute to Victor Bonney

PRESIDENT'S ADDRESS

By DOUGLAS MACLEOD, F.R.C.O.G.
London

WHEN I was apprenticed to Victor Bonney in 1928 as Resident Surgical Officer at Chelsea Hospital for Women, I was schooled in certain surgical procedures which in their day were considered to be the ultimate, but which over the years have been modified by experience and by a careful surgical survey of the results of such procedures.

In this Address I shall take a few sample operations and compare the thought and technique of thirty years ago with our modern standard practice.

Before I select these few surgical procedures, it is appropriate to consider the technical advances in gynæcological surgery which have been achieved during my active surgical career.

Anæsthesia

When I was a house surgeon, the standard gynæcological anæsthetic was an induction by open chloroform and ether or a closed circuit Clover in which the patient was intoxicated by her own carbon dioxide and from which state she was ultimately promoted, as an act of grace, to open ether administered on six layers of gauze. The saturation point was reached when the frozen crystals encrusted the cage over the patient's face with a miniature Matterhorn. To the more youthful this procedure may seem fantastic, but it is true and Victor Bonney (1952) has already paid testimony to the expert administrators of this form of anæsthetic, who made his major surgery possible.

The young operator of to-day should pause and consider how much he owes to his expert anæsthetist colleague; the extended operation that he light-heartedly performs in 1958 is less a tribute to his surgical skill, than an acknowledgment of the splendid and spectacular advances of the sister art of anæsthetics.

This acknowledgment increases the stature of my old surgical chief, who in an anoxic and congested patient, poisoned and drugged with chloroform and ether, was able to complete, with no relaxant whatsoever, a complicated operation in the pelvis. A natural off-shoot of the situation was a predilection for spinal anæsthesia, which at least gave the surgeon some relaxation. One senior surgeon at The Chelsea Hospital for Women never operated with a relaxed rectus muscle and the sole and total effort of his assistant was concentrated on separating the rigid abdominal muscles. Let those who operate now with abdominal musculature so slack as to render retractors unnecessary and with the gut discreetly unobtrusive realize the difficulties of their surgical predecessors.

Resuscitation

The pioneer work on uterine cancer "carved out" by Victor Bonney owed nothing to blood transfusion, which in his first 400 cases was itself a major surgical event. The performance of an extensive pelvic operation, handicapped as it then was by a primitive anæsthetic, was indeed heroic enough, and if hæmorrhagic shock demanded a blood transfusion this codicil was almost as major as the original operation. It involved the summoning to the bedside of the patient a panel of potential donors, relatives, friends, neighbours and well-wishers. When the select coterie was convened, the house surgeon and registrar performed a simple compatibility test on a white tile such as may be found in any hotel bathroom.

If the donor's corpuscles and the recipient's serum were not obviously antagonistic, the transfusion proceeded with a clear conscience, irrespective of the niceties of Rh-compatibility and the possible hazards of subgroup reactions.

That some of us who are "old stagers" knew something of the hazards of incompatible transfusion, such as rigor, jaundice and anuria, is not surprising in the light of modern technical advances, but these we regarded as part of the game and all in a day's work.

The willing donor was rapidly bled with a large calibre French's needle or an open vene-

FIG. 1.—The Kimpton tube.

section into a paraffined prepared glass receptacle, known as the Kimpton tube (Fig. 1), and more often than not, massive clotting would occur like a flash throughout the whole column of blood. The patient house surgeon, with a sigh of frustration, would then set about bleeding the next relative, while meantime the patient's condition deteriorated — often past redemption.

The more advanced intravenous therapists of our particular era were enthusiastically poisoning their patients with water and salt, so that something at least was going into the vein while the blood was being collected. The only colloid available for intravenous therapy was a lethal mixture of gum acacia.

Let it therefore be remembered by those who now light-heartedly tackle the anæmic patient that our gynæcological forefathers relied on speed and not blood replacement for their shocked and anæmic surgical problems. Only in the last 100 of Bonney's 500 Wertheim operations did blood transfusion play any significant part, and his overall mortality of 14% should be interpreted in the light of this significant factor. The modern Wertheim operation, carrying a mortality figure of 2% or less, is merely a tribute to the genius and skill of a great pioneer.

Paralytic Ileus

A number of mysterious post-operative complications and deaths dogged our old chiefs for no apparent reason, as straight-forward operations "went bad on them". A sinister ileus, unexplainable by pelvic peritonitis, frustrated and nullified the best surgery. Some of these obscure complications were thought to be due to the "ileus duplex" of Sampson Handley but we now know that many of these obscure conditions can be explained by a post-operative dysequilibrium of water, salt and potassium. The modern patient rests happily under the benign protection of the flame photometer, and dangers of hyper- and hypo-chloræmia and -kalæmia hold no fear for her.

There is little doubt that the enthusiastic administration of salt and water poisoned and killed many patients in the early 1930s, and the assessment and control of a correct ionic balance is one of the major advances in the comfort and safety of the post-operative state.

As an example of this, let us consider the treatment of paralytic ileus thirty years ago. Progressive vomiting, distension of the gut with a rising pulse, dehydration and, though it was not then realized, dechloridation, presented to the simple mechanistic minds of our chiefs one possible solution, a laparotomy. Fearlessly they opened the abdomen, to be assailed by coils of distended small gut. Into this complicated morass they plunged with dauntless courage, quite ignorant of the real condition with which they were trying to cope. The more courageous performed perhaps an ileostomy, but all were happy to congratulate themselves if they even closed the abdomen at all. Such an operation, not uncommon in our youth, never occurs now. The intestinal suction tube of Miller-Abbott or Cantor has completely revolutionized this fantastic surgical nightmare, and retrograde intestinal decompression is one of the most signal advances of the last quarter of a century. No surgeon now is called upon to open the abdomen for post-operative distension due to paralytic ileus, providing that he has been able to exclude the possibility of organic obstruction.

Chemotherapy and Antibiotics

Until 1935, any woman who was normally confined ran the appalling risk of being cut short in her prime by the dreaded scourge of puerperal infection. Similarly, abortion, however innocently occurring, or any surgical operation carried with it the risk of serious illness or death from the hæmolytic streptococcus. The answer to this condition in those days was a feeble and inadequate gesture by surgery, polyvalent antistreptococcal serum or even a vaccine. The advent in 1935 of red Prontosil and the establishment in Ravenscourt Park of the Isolation Block of Queen Charlotte's Hospital under Leonard Colebrook revolutionized the treatment of the puerperal and surgical septic patient. The first drugs were crude, toxic and unpleasant, but the therapeutic advance was rapidly perfected by the advent of a whole series of potent sulpha drugs which saved countless lives in the Second World War. This was the year when I first entered St. Mary's Hospital as Assistant Gynæcologist and many were the discussions at the lunch table on the merits of the new drug. It was at one of these lunches that I first met Professor Alexander Fleming (Fig. 2), who rather plaintively said to me that "he had something far better than Prontosil, but he could get no one to take any interest in it". He told me that he had called it penicillin and took me up to his laboratory and showed me the original culture plate (Fig. 3). He even suggested that I tried the effect of the mould for vaginal infections, which I did but

FIG. 2.—Alexander Fleming.

Reproduced from Fleming (1929) by kind permission

FIG. 3.—Fleming's original culture plate showing the dissolution of staphylococcal colonies in the neighbourhood of a penicillium colony.

with no result, as the mould was rapidly destroyed. It was not until nearly eight years later—in 1943—that the British antibiotic, penicillin, was made available to the Armed Forces and at the end of the war penicillin was eventually available to the whole population. What a debt we owe to Professor Fleming, who discovered what has now become a universally available drug of immense potency for the good of all humanity. Fifteen years ago, no such drug existed and many lethal organisms menaced the gynæcological patient, taking a toll of all elective operations. Nowadays, no house surgeon cares a damn for a streptococcus—he merely regards the penicillin-resistant *Staphylococcus aureus* as rather a bore. It is fitting and proper that we should realize that our carefree attitude to the problem of pelvic sepsis has been absoutely revolutionized by two British scientists working at St. Mary's Hospital, Professor Colebrook and Sir Alexander Fleming.

Having briefly sketched the changing events against which our modern gynæcological technique has been evolved, I now propose to select a few surgical examples of what was then the standard procedure and compare them with what we do now.

Uterovaginal Prolapse

Prolapse in London must be a very gentle affair compared with the impressive visceral extroversion of a Lancashire mill-hand. The fertility of the stout North Country lass, in combination with long hours spent tending the looms, produced a problem which only a North Countryman could solve. The vaginal approach of Donald and Fothergill to an essentially vaginal problem demanded a considerable knowledge of the anatomy of the pelvic fascia and musculature. Few surgeons trained in the abdominal philosophy of Lawson Tait, Spencer Wells and Bland-Sutton, were able, or cared, to grasp the importance of a pelvic fascial and muscular reconstruction which had been developed as a result of the enforced confinement of the gynæcologist to the vagina by the jealous bailiffs of abdominal surgery.

In many hospitals, at the turn of the century, the obstetrician/gynæcologist was forbidden to open the abdomen, and the diagnosed presence of an ovarian tumour automatically called in the general surgeon. The restriction of surgical activity, evil as it undoubtedly was, did ensure great agility and ingenuity in operating on the pelvis through the vagina, and it is possibly this archaic limitation which bred the great vaginal plastic surgeons who perfected what is now considered the standard operation for uterovaginal prolapse—the Manchester operation.

A certain happy rivalry existed between the North and South, and the Southerners who were unable to repose the prolapsed womb from below countered this challenge from Lancashire by hitching it up from above, and so the famous

"round trip" or circular tour operation was invented and became, at Chelsea Hospital for Women, almost the standard procedure for vault prolapse (Tables I and II).

TABLE I.—CHELSEA HOSPITAL FOR WOMEN 1929

Operations for prolapse		162
"Round trip"	47	
Ventrofixation (alone)	27	
Le Fort	11	
Shortening round ligaments (Gilliam)	60	
Fothergill	10	
Colporrhaphy (alone)	7	

TABLE II.—CHELSEA HOSPITAL FOR WOMEN

Operations

Mr. Rivett (September 27, 1929)

1. Classical Cæsarean section
2. Colporrhaphy, perineorrhaphy, ventrofixation for procidentia
3. Perineorrhaphy and ventrofixation for procidentia

The "round trip", as it was rather vulgarly known, consisted of a token anterior and posterior colporrhaphy: token is the operative word, since the colporrhaphies consisted in excision of a diamond or triangle of redundant vaginal skin and a few timid nibbles at the levator ani. The cervix was left severely alone and the mysterious Mackenrodt's ligament remained untouchable. This little vaginal job took perhaps twenty minutes and our gynæcological fathers now emerged from the obscurities of the nether regions to a territory which they understood. Happily changing gown and gloves, they opened the abdomen through the mid-line with one sweep of the knife, seized the body of the uterus and pulled it upwards. Calling for the stoutest available silk, they transfixed rectus muscle fascia, peritoneum and womb in one. This suture was passed three or more times and after tying, it only remained to suture the skin. This abdominal encore could be performed in no time at all, and the immediate end result was spectacular. A vaginal examination performed on the patient's discharge disclosed the cervix only to those endowed with a long finger—and mutual congratulations completed the job. However, the ventrofixed uterus, when parous, was not without danger. The more thoughtful and critical minds, in due course, became somewhat disturbed at a harvest of ventral herniæ, vicarious incisional menstruation, stitches removed from the endometrial cavity by a curette, intestinal obstruction due to utero-abdominal bands and a progressive hypertrophic elongation of the cervix and some very remarkable herniæ of Douglas's pouch. The cervix performed a Pilgrim's Progress, eventually reaching the introitus, although the fundus might still be secured to the abdominal wall. The bladder resented the restriction of its new antomical relationship and produced a distressing inability to expand.

As time passed, patient and surgeon realized that the "round trip" was not worth the fare—and this particular bus route was eventually withdrawn from service.

From what we now realize was primitive prolapse surgery, there evolved the clear and simple concept of the Manchester operation and its establishment as the standard technique.

Hysterectomy

The original treatment of fibroids by bilateral oophorectomy was dictated by the staggering mortality of hysterectomy and this operation, now performed totally throughout the country with a mortality of 0·4% and less, in 1925 had a mortality almost ten times greater, for reasons that we have already outlined (Table III). The

TABLE III.—CHELSEA HOSPITAL FOR WOMEN 1929

Abdominal operations		721
Mortality	3·32%	
Non-abdominal operations		814
Mortality	0·61%	
Operative mortality for the year	1·88%	

only real risk of a hysterectomy to-day is phlebothrombosis and pulmonary embolism, and when this last obstacle has been removed our hysterectomy patients should have achieved theoretical immortality.

The quicker and simpler subtotal operation recommended itself to our seniors in the unrelaxed patient and the avoidance of the open vagina removed some of the hazards of ascending sepsis. A crop of ureteric catastrophes by the more adventurous provided strong argument against the total operation. The risks of stump cancer had not been explored and the standard procedure was therefore a quick subtotal (Tables IV and V).

TABLE IV.—CHELSEA HOSPITAL FOR WOMEN 1929

Hysterectomy for benign conditions		222
Subtotal hysterectomy	182	
Total hysterectomy	40	

TABLE V.—CHELSEA HOSPITAL FOR WOMEN

Operations

Mr. Bonney (August 13, 1929)

1. Wertheim's hysterectomy
2. Subtotal hysterectomy
3. Subtotal hysterectomy
4. Subtotal hysterectomy
5. Ovariotomy and ventrofixation for ovarian cyst and procidentia

The evolution of the total operation has taken time and the subtotal operation is now becoming a rarity or should be. The residual cervix is of no value, except nuisance value. It provides a focus of subsequent pathology in cervical

erosions, polypi and malignancy; it does not discourage vault prolapse; it is not the keystone of a theoretical arch and its presence does not guarantee any more sexual satisfaction than its absence. The menace of stump cancer, though small, is real, and treatment by radium or surgery is inadequate and depressing.

Cæsarean Section

A retrospect of Cæsarean section over the last thirty years is instructive and interesting. The classical operation in the speedy and expert hands of the Chelsea Hospital staff still had a dread mortality of 2%, which was ten or twenty times greater than natural delivery, and in suspect and infected cases this mortality was multiplied many times.

For the busy gynæcologist/obstetrician, Cæsarean section was a wonderful escape road which secured some leisure at the week-ends, and the indications for its performance became even wider. At one London teaching hospital a woman might congratulate herself if she brought up her family without the tell-tale scar 1 in. above and 2 in. below the umbilicus. General surgeons, when faced with a problem of intestinal obstruction, always learned to look for this incision which was a site of predilection for small gut adhesions. The speed and ease with which a classical Cæsarean section was performed ($6\frac{1}{2}$ minutes from the first cut to the last clip) held the onlookers spellbound and provided the material from which much of what we now know about paralytic ileus was learned. Any primigravida and many multigravidæ in whom the fœtal skull was not safely out of reach of these surgical enthusiasts had her case-notes marked "disproportion—for Cæsarean section at term".

Some of you know the story of a famous Cæsarean exponent who had opened the uterus and extracted the breech, but was unable to withdraw the head from the pelvis until a kindly colleague dislodged it from the vagina. This state of affairs—rather comparable to the "round trip"—gave rise to a Cæsarean section revulsion, and in the next era no obstetrician was considered worth his salt unless he could extract the impossible from the vagina, and a rival institution to the one above—not mentioned—would submit a woman to five days' hard labour ending, if necessary, in a dead baby rather than employ the simple expedient of abdominal section. Maternity units began to grade themselves according to the smallness of their Cæsarean rate and a prize was universally awarded by popular assent to the hospital which did the fewest sections. The advent of the lower segment operation, in which Munro Kerr and Victor Bonney both played an important part, somewhat restored the surgical safety of the operation to the suspect and even infected patient. The fact that young obstetricians were taught that one vaginal examination meant no Cæsarean section shows the extent to which post-operative puerperal sepsis was dreaded. In the late 1930s, the well-equipped obstetric surgeon performed a classical Cæsarean section on the elective indications, while he prided himself that the suspect or infected cases were delivered by the lower segment. Victor Bonney regarded the classical operation as a bloody procedure which was surgically inartistic and unsound. He dubbed it a "smash and grab raid" in a Bradshaw lecture and from this time onwards he proceeded to perform elective section through the lower segment on the women in labour. He used his compressor, designed to prevent bleeding from the uterine incision—and very effective it was (Figs. 4 and 5) (Bonney, 1933).

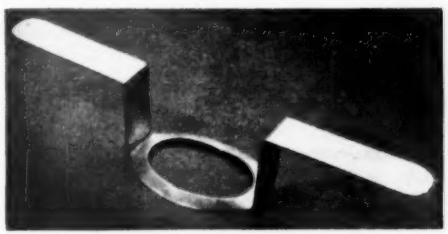

FIG. 4.—Bonney's uterine compressor.

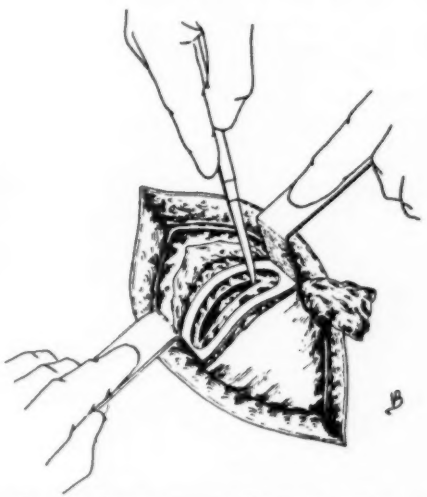

FIG. 5.—Lower segment Cæsarean section. Incising the lower segment in the area bounded by the compressor. Reproduced from Bonney (1952) by kind permission.

Bonney was a man who thrived on his critics and several were quick to challenge the presence of a lower segment at all in a woman who was not in labour. According to them Bonney was performing an operation through a part of the uterus that did not exist. Undeterred by this academic counter-fusillade, Victor Bonney continued to use the lower approach and, as his pupils soon realized the surgical safety and lesser hæmorrhage inherent in the lower regions, the technique gradually became recognized and perfected.

The die-hards, however, refused (and some still do) to perform a lower-segment operation. The argument of sepsis in Cæsarean sections, by whatever route performed, was eventually resolved by Leonard Colebrook and Alexander Fleming, neither of whom was likely to have performed a Cæsarean section in his life.

Obstetricians can now put the operation in its proper perspective, and its relative safety—thanks to antibiotics, and advancements and refinements in pre- and post-operative management—allows it to be performed with a mortality approaching that of vaginal delivery. The perforator, the cranioclast and cephalotribe are now seen only on the examination table in the Final Conjoint and M.B. examinations and candidates are no longer ploughed for not knowing what these museum pieces are.

FIG. 6.—Victor Bonney.

To many of you Bonney must be a legendary figure and in this Address he keeps making his presence felt in the influence which he had on the changing events which I have depicted and one final example will show the great debt which the modern gynæcologist owes to him (Fig. 6). He was essentially a pelvic surgeon rather than a genital tract specialist and the unsurpassed series of over 500 Wertheims taught him every aspect of pelvic anatomy. One cannot perform one Wertheim, let alone 500, without making sometimes unpleasant acquaintance with the adjacent territory of urinary tract and bowel. Lesser men graciously handed over these problems to their brother specialists in urology and proctology; but not so the master, who was as happy and competent operating on bowel or ureter as on the uterus. This catholic outlook in the pelvis involved him in some criticism which once more he was able to survive, and it is now hoped that his doctrine that "he who opens the abdomen should be competent to deal with whatever he finds there" will be accepted by all. This last statement epitomizes the doctrine of the modern pelvic surgeon, and it is an ideal which should not be surrendered to the party politics of narrow specialization.

Wertheim's operation which Bonney perfected and which was his pride and joy was in those days the only effective treatment for carcinoma of the cervix. Radium was but in its infancy, but as technique improved, so did the results, till the time came when not only did they equal but even surpassed those of surgery. It was at this time that radiotherapists challenged the sovereignty of the surgeon in this realm of gynæcology and heated and often bitter discussions took place in this very hall. A time came in 1937 when it was actually stated that the Wertheim operation as a treatment for cervical cancer was now obsolete (Bourne and Williams, 1939). However, this is not true to-day. Wertheim hysterectomy still holds a place in the treatment of selected cases and for those which appear to be unsuitable for irradiation.

That Wertheim's hysterectomy is no longer considered the accepted treatment of carcinoma of the cervix is not surprising to me. For many years I have been unhappy over one detail of technique—the dissection of the ureter as it passes through the para-cervical tissue in the ureteric canal. I was not convinced that if spread had occurred in this situation, it could be completely eradicated by this means.

In a few early cases, where clinical evidence of parametrial extension was absent or minimal, I deliberately divided the ureter, removing the lower 2 in. (5 cm.) together with the parametrial tissue, and reimplanted the proximal end into the

FIG. 7.—Uterus and vagina removed by Wertheim's hysterectomy showing resected portion of both ureters.

bladder (Fig. 7). The parametrium, together with the segment of ureter, was examined by serial section and in one case a minute node, less than 2 mm. in diameter and invaded by cancer cells, was found lying adjacent to the ureter (Fig. 8).

achieved by irradiation alone remains to be seen. Though surgery is no longer the accepted treatment for cervical cancer, there is to-day a renaissance of the Wertheim operation. Winterton, Bonney's penultimate registrar, is now practising the operation in the treatment even of carcinoma of the body—a logical procedure since the extended operation has eliminated some of the commoner sites of recurrence and should improve the five-year cure rate.

This advance would make my old chief blanch, for he never intended the Wertheim to be used except for cervical cancer, but he would be the first to appreciate this logical approach.

Let those gynæcologists who now perform this extensive operation in the safety and comfort of modern advances not forget that what they are doing was regarded as obsolete, dangerous and unjustifiable in 1937, except by one man, who bided his time and continued steadfast in face of overwhelming opposition, and saved from the scrap-heap a piece of surgical technique which still remains of utmost importance to the cancer patient.

FIG. 8.—Microscopic section of parametrium showing a minute lymphatic node invaded with cancer cells.

The chance of completely removing all trace of cancer in such cases must be small indeed and this is borne out in Bonney's report that 50% of recurrences following Wertheim's hysterectomy occur in the mid-pelvis. Full irradiation preceding Wertheim's hysterectomy as practised by Schlink, Stallworthy and others would appear from these findings to be a logical approach, but whether a Wertheim's hysterectomy after full irradiation will in fact improve on the results

What started out as an examination of the changes which have taken place over the last quarter-century has, inevitably and unconsciously, become a tribute to my old chief. No pupil need ever apologise for applauding his teacher, and there can be few of us in this room who do not owe our present position to the inspiration and stimulation of a great mind.

Those of you who have patiently followed me in this Address will have discerned the debt that

in our everyday surgical practice we owe to the great pioneers of pelvic surgery, and while we pay tribute to their originality of thought, a close appraisal of some of their best ideas has shown them to be untenable by modern standards. The obsolescence of ventrofixation, subtotal hysterectomy and classical Cæsarean section is an example.

The fact that our fathers sowed a few "surgical tares" should not fill us with complacency, or satisfaction in the present achievements of our own pelvic surgery. For somewhere in this hall there probably sits one who will be standing here in my place in thirty years' time, and who, when surveying the scene of surgical progress will marvel at the crudity and ineffectiveness of our present practice. With pity and incredulity he will recount how the pioneers of the 1950s performed their archaic operations under conditions of anæsthesia so crude as to be laughable in the enlightened 1980s.

Let this sobering thought encourage us to examine the philosophy upon which our surgery is built, to ensure that the technical performance of it is both thoughtful and progressive.

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Meeting
November 28, 1958

THE following specimens were shown:

(1) **Hæmatometra Twenty-nine Years after Radium Treatment of Carcinoma of the Cervix. (2) Contraceptive Pessary Embedded in the Uterus Necessitating Pan-hysterectomy.**—Miss ALICE BLOOMFIELD.

Five Cases of Malignant Melanoma in Association with Pregnancy.—Mr. ARTHUR WILLIAMS (introduced by Mr. J. STALLWORTHY).

Tuberculosis of the Vulva.—Mr. JOHN P. ERSKINE.

Two Cases of Rapid Degeneration of Submucous Fibroids.—Mr. HAROLD MALKIN.

Squamous Cell Carcinoma of the Vulva Arising in Condylomata Accuminata.—Mr. MOSTYN P. EMBREY.

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Section of the History of Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., C.B., M.A., D.M., F.R.C.P.

Meeting
December 3, 1958

John Sheldon, F.R.S., and the Exeter Medical School

By NORMAN CAPENER, F.R.C.S.
Exeter

EXETER is an ancient City and was a provincial metropolis. It is, therefore, natural that we should find mirrored there many of the features of medical evolution which are familiar in the great national metropolis itself. It is my purpose to give an account of a place rather than of a man although the particular man, John Sheldon, F.R.S. (1752–1808), is one of the more picturesque features in this interesting background. It is exactly one hundred and fifty years since he died.

From mediæval times until the eighteenth century hospitals differed greatly in their functions. Some were little more than orphanages, or were hostels for the aged poor and in the course of time became schools and almshouses. Some were used for the isolation of destitute individuals suffering from such diseases as leprosy which made them a danger to the community. When Exeter's Norman Cathedral was completed in the twelfth century each of these types of hospital was already established there and has continued in some form or another until the present time. Notable amongst these was the Hospital of St. Mary Magdalene, which is recognizable as a leper hospital in a Charter of Bishop Bartholomew in A.D. 1163, confirmed later by a Papal Bull of Celestine III in 1192. This hospital was established just outside the city wall on a road, still called Magdalen Street, which was a mediæval by-pass for traffic to the frontiers of civilization which were but a few miles farther on. There is thus a resemblance in time and possibly in early function to St. Bartholomew's and St. Thomas's—both outside the city walls and on the main line of communications: but there the resemblance ceases for the Hospital of St. Mary Magdalene in due course became a refuge for the aged sick and itself fell into decay; the foundation, however, in the nineteenth century was moved to a new site and is now represented by some old almshouses which retain their ancient name.

Hospitals were also needed during and after wars. Such is the origin of Chelsea Hospital. They were often arranged by improvisation; with requisition and billeting. The archives of Exeter provide an interesting illustration of this. In 1688 William of Orange landed at Torbay and with thirteen thousand men marched on Exeter which he entered "amidst the shouts of its citizens". There exist lists of some of the casualties and the cost of treatment by the surgeons, apothecaries and by Widow Westcott (evidently the nurse in charge) at the Blue Maidens Hospital. Then there is an appeal in 1706 to Queen Anne requesting payment of the account which William evidently had forgotten. "Whereas your Majesty's Predecessor, King William of ever blessed memory (when Prince of Orange) did a little after his landing at Torbay desire the Chamber of Exeter to take care of part of his Army (Which there lay sick and disabled in and near this City) and to furnish them with necessaries. At the same time promising to reimburse the Chamber with such sums as (by them) should be, on this Account, expended." The expenditure is stated to be £354 4s. 2½d. The Blue Maidens Hospital which had been converted into a Military Hospital was one of the mediæval schools and is now the Maynard School, an excellent grammar school for girls.

In mediæval times there existed an Exeter Guild of Surgeons which is noted in the records of the Guildhall but no records of the Guild itself remain.

Although it is usual to look for the origins of our modern hospitals in the eighteenth century we note that the public conscience was being aroused in the century before. At an early date the City fathers were making efforts to do something, and in 1656 there was a bequest by the Mayor, Thomas Ford, which was "towards erecting a hospital for poor, sick and wounded persons according to the order of St. Thomas's Hospital in Southwark". The first Exeter Hospital so called was built by the commonalty in 1665 and a new hospital was planned through an Act of Parliament passed in 1694. This second Exeter Hospital, completed in 1718, remained until 1942 when the old buildings were

destroyed by enemy action. Later nineteenth century and more modern buildings now form the nucleus of a good modern general hospital.

This old Exeter City Hospital within a few years came into conflict with a new and more broadly based institution established by charitable enterprise. Perhaps we see in this the roots of the deep prejudice of Englishmen against submitting their bodies to the care of municipalities, but perhaps even more against being compelled by taxation to do something more rightly to be regarded as a matter for conscience and as an object for the display of pity and benevolence.

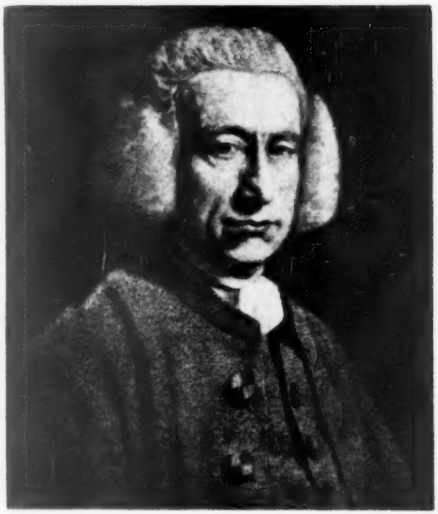

FIG. 1.—John Patch, Jr. (1723–1787). Engraving after portrait by John Opie, R.A.

[Figs. 1, 2 and 3 are reproduced by permission of the Governors of the Royal Devon and Exeter Hospital.]

The Devon and Exeter Hospital was founded in 1741 by Dean Alured Clarke who, in 1736 while at Winchester, had founded one of the first County Hospitals. It was a time of great social degradation, which was well portrayed by Gay in his "Beggars' Opera". The *Gentleman's Magazine* contains many interesting details; for example in 1736 it recorded an incident but a short distance from this Society's House in a list of births: "A woman in Vere Street—of her 35th child by one husband." And in almost every month of that year we see that the burials were at least double the christenings, and half the burials were of infants under 5 years. There was great anxiety about the iniquitous gin trade. The Wesleys had started their crusade and the conscience of the Church was aroused. During this social awakening other Hospitals were founded. In London Bart's, Thomas's, Bethlem and Chelsea already existed, but in succession Westminster—1719, Guy's—1725, St. George's—1733 and the London Hospital—1740, were established. At Edinburgh, Bristol and Winchester, hospitals were founded in 1736 and at Bath the Mineral Water Hospital in 1740. The Devon and Exeter came in 1741. All these hospitals existed long before those at Liverpool, Manchester or Newcastle and before Addenbrooke's, the Radcliffe, Middlesex or St. Mary's.

The first physicians of the Devon and Exeter Hospital were men of great learning enriched by study abroad and especially with the great Dutch teacher Boerhaave. They included Michael Lee Dicker, a Quaker with well-marked administrative ability, and Thomas Glass, a greatly loved and respected physician who collected a great library of the medical classics which he left to the Cathedral Library. Around him there appears to have been established a Medical Society but apart from the fact that there was such a society no record of its activities remains. He was succeeded in 1783 by another physician of great literary ability, Dr. Bartholomew Parr, F.R.S. (1750–1810) the author of a great "London Medical Dictionary".

The earlier surgeons appear to have been worthy men but we know little about their work. John Patch, senior, had been on the staff of the Old Pretender in Paris and was a considerable anatomist; he was the head of a medical dynasty in Exeter and London. His son John was appointed to the Hospital at the same time as his father: as a surgeon he made a great name for himself; his portrait by John Opie makes one understand that "he had a prodigious memory, great penetration and sound judgement and his conversation charmed by its warmth and benevolence".

Through their portraits now in the Hospital board room we are brought into touch with interesting figures in the world of art and letters. Michael Lee Dicker and John Tuckfield, an early benefactor, were painted by Thomas Hudson who was the master of Joshua Reynolds, the Plympton boy who became the first President of the Royal Academy.

Thomas Glass and John Patch, junior, were painted by John Opie, the poor Cornish prodigy who had been befriended by John Wolcot (the satirist "Peter Pindar"). Brian Hill (1954) gave an entertaining account of these two men. Wolcot who came from South Devon was alternately a parson and a doctor but later devoted himself to teaching, and then managing, the youthful artist. Having exhausted the

portraiture of the county families of Cornwall, Wolcot brought Opie to Exeter for two years before going on to London and introducing him to Sir Joshua. Here Opie needed no further help after Sir Joshua's introduction to the Court. It is sad to find that after a journey to Paris for study his later portraits were lacking the distinction of his earlier work which Reynolds described as "like Caravaggio only finer".

We should note that when the Devon and Exeter Hospital was founded in 1741 William Hunter was 23 years old and his brother John 13. Four years later the Surgeons' Company in London separated from its unhappy association with the barbers. Cheselden soon followed Ranby as Master and a few years later William Hunter and Percivall Pott became associated as Masters of Anatomy. In 1746 William Hunter had brought back to London from France the Paris method of teaching anatomy by individual student dissections. In 1748 at the Windmill Street School of Anatomy he was joined by his brother John, who went to Portugal in 1760 and after three years returned to London to establish himself independently.

A link with William and John Hunter and with Exeter is now to be found in John Sheldon, an erratic genius whose work and influence deserve to be remembered more than the doubtful episode with which his name is unjustly more commonly linked.

John Sheldon

John Sheldon was born in 1752, the son of an apothecary-surgeon in Tottenham Court Road, and at an early age was apprenticed to Henry Watson the anatomist who enthused him with his methods of injecting bodies and started him upon experiments in embalming. For clinical training he was a pupil at the Westminster and Lock Hospitals. In 1774 he succeeded Hewson, after his premature death, as resident pupil to John Hunter and attended William Hunter's school. In 1775 he gained the diploma of the Surgeons' Company and was appointed to the staff of the Lock Hospital. He had as one of his patients a young woman of 24 suffering from phthisis to whom he became very attached and before she died she asked him to preserve her body. This he did and removed the embalmed body to his house. In 1776 he was appointed lecturer in William Hunter's school and was so successful that the next year he opened his own school in Great Queen Street, Lincoln's Inn Fields. Although he was only 25 years old he was one of the leaders of his profession and the outstanding teacher of his generation. At his school he gave lectures in anatomy, physiology and surgery and the published prospectus notes his appointment as "surgeon to the General Medical Asylum, St. Marylebone". In it he also announced special financial assistance to former pupils of Magnus Falconer, another Hunterian disciple who, after establishing his own school of anatomy, had, like Hewson, died prematurely. In 1779 Sheldon founded a medical society of which he was the first president: there were about 150 members in London and the provinces and it carried on for several years. More important than that there were four presidents who were governed by the rule that each must "wear his hat while in the chair", is the fact of there being such a society within five years of the founding of the Medical Society of London. When 31 he succeeded William Hunter as Professor of Anatomy to the Royal Academy and was the next year elected a Fellow of the Royal Society and married the daughter of a Devonshire parson.

Sheldon was not a prolific writer. In 1781 he edited a catalogue of Camper's works, and in the following year an edition of four dissertations by Lieberkühn. At this time he was preparing his work on the lymphatic system. Sheldon's work was evidently very well thought of by the Italian anatomist Antonio Scarpa, for the latter made for the work a drawing of one of Sheldon's injected specimens. It is said that Sheldon was the first to shape the cannula as seen in a modern hypodermic needle. The resemblance is certainly very striking. In Sheldon's description of his bevelled injecting pipes he said "I would recommend" that they should be "formed in a particular manner, which I contrived many years ago, for passing into small vessels, especially veins. This improvement consists in shaping the ends of these pipes like the mouth of a pen, taking care to make the edges and point blunt to avoid cutting the vessel when we introduce them". He stressed that these pipes as he called them must be made out of solid well-tempered wire which was drilled out—he had no use for tubes made from flat metal folded over and soldered. He fully explained his own methods, and for this reason the book was praised by Jesse Foot in words that were taken from Sheldon's own introduction and of which the following is an extract:

> "Prefixed to this my first essay on the absorbent system, there is also a chapter on the method of discovering, injecting and preparing these vessels, with a plate of the lymphatic injecting tube, which will prove useful to all who wish to prosecute these inquiries. This unreserved discovery, I flatter myself, will induce other anatomists to publish with their works, whatever they know respecting anatomical pursuits, or investigations; for the progress of the science has undoubtedly been much impeded by

the mystery observed among anatomists respecting the composition of their injections, and their method of dissecting, injecting and preparing the different parts: a mystery which deserves the severest censure, and is unworthy of the character of a philosopher or a man."

He also wrote of the pleasures of discovery as found in the writings of Asellius who first discovered the lacteals: "The natural and simple manner in which Asellius expresses himself, faithfully represents . . . his astonishment, and gives an idea of the sensation which all anatomists experience at the instant of making any interesting discovery." Again: "I have now finished the whole of the anatomical encheiresis and discovered, without reserve, every circumstance which may prove useful to those, who wish to trace and prepare the absorbent system. The height of my ambition will be to increase the number of practical anatomists, and to raise a spirit of emulation among them, which may tend to the further progress of the science, particularly in this important and hitherto almost unexplored, track of anatomical knowledge."

Sheldon never completed the second volume for his attention was distracted elsewhere, which was a great pity, for as Miss Dobson (1954) says, it was a most learned treatise that corrected many previous errors. Had he completed it he would have been remembered rather than Cruickshank as the earliest English authority on lymphatics. Cruickshank who had worked with Sheldon published his work two years afterwards and strangely made no mention of Sheldon's pioneer work which was remarkable when compared with Sheldon's own generous acknowledgments of other workers. For example, he mentions "the illustrious Haller . . . immortal Hewson . . . the late most accurate Mr. William Hewson . . . my indefatigable predecessor the late Dr. Hunter . . . the ingenious Mr. Cruickshank . . . ingenious Mr. Falconer . . . immortal Harvey . . . that lynx-eyed anatomist Lieberkühn". Surely this was a great and generous man.

Sheldon was carried away by other enthusiasms. The first was ballooning. In 1782–3 the brothers Montgolfier and other Frenchmen had carried out their pioneer flights. Sheldon himself made an unsuccessful experiment. In 1784 Blanchard, who first had used a condemned criminal as an experimental animal for his ballooning trials, carried out several ascents himself and then came to England and in partnership with Sheldon made an ascent. Blanchard was greatly piqued because he wanted to make the ascent himself and appropriate all the glory. After rising a short distance, with various instruments which Sheldon took for scientific investigation, the balloon came to earth and Blanchard is reported to have exclaimed "If you are my friend you will alight. My fame, my all, depends on my success". Sheldon, however, was determined to continue the journey, whereupon Blanchard "in a violent passion, swore that he would starve him and threw out all the provisions". It was commented at the time that this was a good French notion to get rid of an Englishman. Sheldon, however, still insisted on continuing the journey and the balloon, lightened by the loss of the food, rose again and passed over Hammersmith, Chiswick and Twickenham and gradually descended near Sunbury. Here Sheldon did alight and Blanchard went on to Romsey 73 miles from London to which Sheldon followed on horseback and they returned to London together the following day.

In 1784 when he was elected a Fellow of the Royal Society he was visited by Monsieur Saint-Fond, Professor of Geology in Paris who later reported his visit to Sheldon's Museum, in which the most interesting exhibit was the mummy already mentioned. "It occupied a distinguished place in the chamber where the anatomist usually slept." It lay in a mahogany table with a glass top and Sheldon demonstrated to him the perfect preservation and flexibility of the parts of the body. Even the skin partly retained its colour, though exposed to the air. Sheldon explained how he had carried out the embalming ten years previously and he stated that "the remains were those of a mistress whom he tenderly loved".

After his death his widow offered the mummy to the Royal College of Surgeons where it remained until destroyed by enemy action in 1941. Many apocryphal stories have been told about the identity of the lady in the case. Sir D'Arcy Power stated that he often used to visit her in the College basement but the body could not then have been very beautiful, for it was "shrunken and hard as a board, the skin of the arms, neck and chest quite white; the face, where apparently the colour injected had remained, a dull red all the more ghastly for its colour and the long brown hair beautiful no more".

The episode of Sheldon and the mummy of his supposed mistress has, I maintain, been magnified into a piece of scandal on the evidence of only one perhaps rather imaginative witness. Rather than this being a labour of love I regard the actions of Sheldon's wife and his own character, as seen in his writings, as proofs that what he achieved was a work of art and science in a field which at that time dominated the whole of medical and surgical progress—the convenient study of anatomy.

In 1786 Sheldon was appointed surgeon to the Westminster Hospital and was a leader in his

profession, with his own teaching school and his own museum, a recognized authority on lymphatics; and it is incomprehensible why he should have abandoned all this a year or two later. One story has it that his museum was attacked and demolished by a mob before the troops arrived. With John Hunter, Sheldon was interested in the anatomy of whales and devised a poisoned harpoon for capturing them. In the spring of 1788 he set off for Greenland and on the journey contracted what was called brain fever. His illness was long and he retired to Devon to recuperate with one of his sisters. On hearing this Cruickshank attempted to secure the Professorship at the Royal Academy but Sheldon's brother Thomas and his sister petitioned the Queen and Sheldon continued to give the annual course of lectures until he died in 1808. In 1789 he published an interesting paper on fractures of the patella which he recognized as being due most commonly to muscular violence. In treatment he stressed that it was necessary to flex the hip in order to relax the rectus femoris muscle. Some of the figures for this work were drawn for Sheldon by Professor Camper and two of the specimens were from William Hunter's collection.

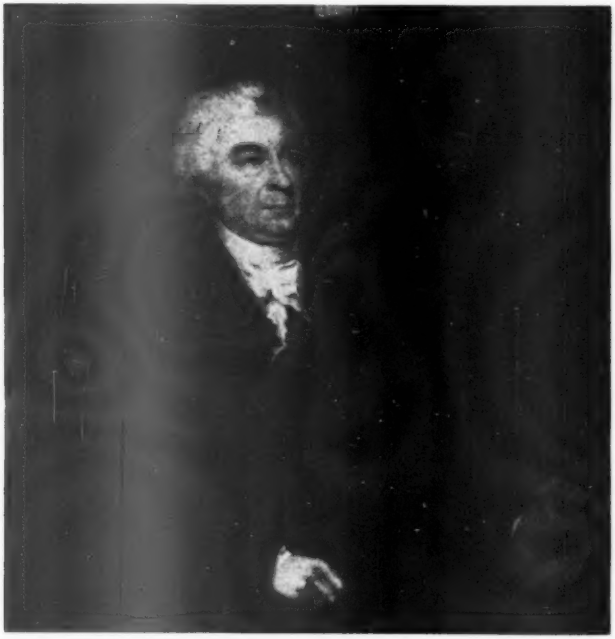

FIG. 2.—John Sheldon (1752–1808) in later life.

In Exeter Sheldon established himself in private practice and in 1796 he contributed an article to a volume of "Essays by a Society of Gentlemen at Exeter". One of the leading spirits in this was Downman the poet and a physician at the Devon and Exeter Hospital. Sheldon's essay was on the structure of the iris with a theory of muscular motion, in which he thought that the fluid content of muscle fibres was merely a continuation of blood vessels which reacted to the stimulus of light and in different states of engorgement contracted or relaxed. Although we may now recognize the fallacy, the idea was not far removed from Sharpey-Schafer's theory of variations in fluid content of muscles, which was the current explanation of muscular action until the beginning of the present century.

In April 1797 Sheldon was the centre of conflict occasioned by his application for the vacancy of surgeon to the Devon and Exeter Hospital upon the resignation of Bartholomew Parr, senior. The voting upon Sheldon, favourable by one committee, was reversed by a Court of Governors: and so it went backwards and forwards four times before Sheldon was finally accepted. His work and character were greatly esteemed by the members of the staff and by the patients. He died aged 56 in October 1808 and is buried in Coombe Raleigh Church, Honiton. In 1809 Jesse Foot wrote: "He was humane, active in every intercourse of friendship, though of so animated a character, mild, forbearing and affable. His conversation was lively as well as erudite and he had a strong sense of humour and great ingenuity in displaying it. There was nothing like envy in his composition; on the contrary, if useful knowledge was discovered by anybody, he was zealous to diffuse it, and to procure due honour for his forebears."

With John Sheldon another interesting character was appointed to the staff in Dr. John Blackall, a physician of enquiring mind, a former student of Bart's and D.M. Oxford who anticipated Bright in relating dropsy to albuminuria and renal disease.

The study of medicine and surgery at this time was largely by means of apprenticeship, in which surgeons had their pupils and physicians their

clerks. Amongst the pupils of Sheldon at Exeter were Samuel Barnes and John Haddy James. Both men came to London and studied at Bart's and both, at different times, were house pupils of John Abernethy.

Samuel Barnes

Samuel Barnes was a brilliant student and later was an outstanding surgeon. He is said to have been the first provincial oculist. He was not a creative scientist but he made an extensive collection of osteology which later formed part of the Medical School Museum that he and Haddy James established. He was a classical scholar with great literary interests which, it appears, were more important to him than his surgery. These led him to become for forty-five years the Secretary of a literary society—the Devon and Exeter Institution—which still exists. He is also to be noted as one of the ancestors of the actress sisters Irene and Violet Vanbrugh.

John Haddy James

John Haddy James was a colourful personality an account of whose life and work has been well written by Rocyn-Jones (1953). After being a student under Sheldon, James was one of Abernethy's favourite pupils and there still exists a very interesting correspondence between the two. He was a house surgeon at Bart's and then became an assistant surgeon in the Life Guards and served at Waterloo of which he gave a most graphic description.

"He left the Army in 1816 on his appointment as surgeon to the Devon and Exeter Hospital . . . and was most assiduous in his hospital duties making careful and copious notes of his cases. He displayed great ingenuity in devising mechanical contrivances to aid in the treatment of injuries by way of special splints, syphons to aspirate exudate from wounds and abscesses, and a device to provide a constant water drip for inflamed surfaces. In 1818 he won the Jacksonian Prize of the Royal College of Surgeons for his essay on 'Inflammation' which he afterwards expanded into a larger work entitled 'On the General Principles and Treatment of Inflammation' which was published in 1821 and followed by a second edition in 1832."

Here I would particularly note the close association of James and Barnes as leaders in improving the educational facilities for medical students at the Devon and Exeter Hospital and in bringing a corporate spirit into this training so as to raise a rather restricted system of apprenticeship into that of a medical school. On January 7, 1819, they petitioned the Devon and Exeter Hospital that it being their intention "to give an annual course of Anatomical Demonstrations to the medical pupils of the place on subjects procured from London for this purpose, they request, in concurrence with the other medical officers of the House, permission to employ the laboratory of the Hospital for this purpose". Permission was readily given. A pathological museum was formed of which James became curator and wrote the catalogue. For many years he and Barnes gave an annual course of lectures on anatomy. James attracted many pupils, of whom some were resident in his house and all were dressers at the hospital.

Fig. 3.—John Haddy James (1788–1869).

"By arranging hospital teaching for the apprentices the Exeter surgeons tended to unite them into a body, thus rendering them only partly subservient

to their individual masters." Based upon the requirements of the Society of Apothecaries in 1815 "it was an early attempt to provide in part a provincial as opposed to an exclusively metropolitan medical education. The same idea of improving the tone of provincial medicine and supplying a medium for discussion and diffusion of medical knowledge induced James and several others to meet Charles Hastings at the Worcester Infirmary in 1832 in order to found the Provincial Medical and Surgical Association. At the inaugural meeting James was elected member of the Council and a paper by him on the diagnosis of strangulated hernia, with some practical remarks on the operation, appeared in the first volume of the Association's Transactions. At the annual meeting held in Liverpool in 1839 he delivered the Retrospective Address in Surgery: in 1842 he was the president of the two-day meeting at the Athenæum in Exeter. James delivered a presidential address and gave clinical demonstrations in his wards at the Devon and Exeter Hospital. It is interesting to note that at the Association Dinner held in the New London Inn on August 4 one of the guests who replied eloquently to a toast was Archdeacon J. H. Pott—son of Percivall Pott."

In 1843 when the Royal College of Surgeons was reconstituted James was elected one of the original Fellows and took a leading part in their affairs.

"James was a good anatomist and pathologist; a careful though not a dexterous operator and on occasion bold. He had a gift for invention, his wards had many original devices designed to promote healing or restoration of function in his patients, about whose welfare he was very solicitous. He made many contributions to surgical literature: besides those already mentioned two others should be noted; one entitled 'Some Contributions to the Pathology of Fibrous Tumours', in two articles in the *Lancet* (1868), the other 'On Ligature of the External Iliac Artery in a Case of Double Aneurism' (1884).

"Early in life he infected himself at an autopsy and became dangerously ill on his way to London; he was treated by Abernethy in his own house. Afterwards James enjoyed robust health until his last five years when he developed glaucoma and optic neuritis which ended in blindness. . . . He modelled himself on Abernethy of whom he was both pupil and friend. He took a prominent part in raising the standard of extra-metropolitan surgery and was a powerful supporter of the movement to bring all members of the profession together into an association for mutual instruction and protection. . . . He had an inventive mind. . . . One of his resourceful inventions was directed towards providing continuous yet tolerable traction in the treatment of skeletal injuries. This he achieved by weight and pulley. The apparatus he described was so simple in design that it was capable of use in any country cottage. The need for continuous traction had long been felt but James's contribution towards its provision was scarcely appreciated. Weight and pulley traction is now a commonplace procedure in surgery but he who had the heart and mind to introduce it deserves to be remembered."

He died on March 17, 1869.

The Medical School

The Minute books of the Governors of the Royal Devon and Exeter Hospital extend back to its foundation in 1741 and are a mine of information upon provincial hospital conditions in the eighteenth and nineteenth centuries. There are frequent references to the house pupils of the apothecary and of the surgeons. The intention to provide some better educational facilities is first seen in 1813 when the committee received a request to form a library and museum: a library trust was established the same year. In 1819 a start was made with the courses upon anatomy already mentioned and these attracted a large number of pupils from Devon and Cornwall, each coming for four or five years. This time was followed by a year in one of the great teaching centres of London, Edinburgh or Dublin. In 1823 courses in chemistry were also started.

An interesting incident of the state of affairs previous to the Anatomy Act should be mentioned. There was keen demand for bodies by the new provincial schools as well as from London. There were organized gangs of body snatchers and it seems that when things were too hot for them in one area the gang moved elsewhere, e.g. from Liverpool to Exeter on one occasion. One wonders whether that had anything to do with the case reported in the *Lancet* in 1824 when Mr. Cooke, an Exeter surgeon, was before the assizes and fined £100 for having received the body of a young woman from resurrectionists who had removed it from the graveyard of St. David's. Wakely, the *Lancet* editor, made an impassioned appeal for help and raised £200 to defray the fine and costs.

In 1827 the Dissecting Room was active in a peculiar way for it was resolved "that the admission of strangers to view the body of a condemned malefactor brought to the Hospital for dissection be allowed on the day of execution only". In 1832 the Hospital applied for a licence under the new Anatomy Act. In 1833 the Government's Inspector of Anatomy recorded the number of bodies used in provincial schools. Manchester had the most with 24. The others were Birmingham (20), Sheffield (19), Liverpool (16), Leeds (9), Bristol (7), Exeter (5), Bath (3), Cambridge (1), Hull (0) and Nottingham (0). Oxford is not mentioned.

In 1834 the Devon and Exeter Hospital was one of the provincial centres selected for enquiry by the Parliamentary committee upon Medical

Education. The pages of the *Lancet* in that year gave an abstract of some of the evidence embellished by Wakely's satire. Abernethy (described by Wakely as "that most subtle knave in medical politics") had said that "many of the provincial hospitals (not recognized by the Council of the Royal College of Surgeons) present a larger field for the acquirement of practical knowledge, than is to be met with in some of the metropolitan hospitals which were recognized as schools of surgery". Guthrie had also mentioned that the Westminster was not the equal of Manchester—the former recognized and the latter not. Later that year the *Lancet* published a protest from 27 pupils of the Devon and Exeter Hospital supported by 38 medical practitioners of Exeter against new regulations of the Company of Apothecaries extending the length of time required in London Hospitals.

In 1851 the surgeons appear still to have been taking the major part in the training of students and they pressed for better accommodation for lectures and the museum. They could get no help from the Governors. The staff then set about collecting funds and raised £650 privately (a large sum in those days). It was enough to build what was needed and provide a small endowment. With the passing of the Medical Act of 1858 the School came to an end but the buildings were still in existence when I went to Exeter in 1931. The Library and Museum, now rehoused, provide the home of the Devon and Exeter Medico-Chirurgical Society which was formed in 1870 as the successor of previous Medical Societies, the first of which is noted in 1783, the Exeter Medical Library Society in 1813, the Exeter Pathological Society in 1832, the Exeter Dispensary Society in 1848, &c.

Exeter Medical Library

The Exeter Medical Library is a remarkable collection and is in two parts, the more important sections of which were housed together at the Devon and Exeter Hospital from 1815 until 1948. The older section goes back to the Middle Ages and is now again part of the Exeter Cathedral Library to which most of it was bequeathed by Dr. Thomas Glass in 1786. The rest of the library which is still at the Hospital has been added to throughout the years from 1815. In 1824 it received the Parr collection, and in 1841 notable additions bought from the residue of a Cholera Fund raised in 1832 to relieve the sufferers from the calamity of that year and which was recorded in a notable epidemiological report by Dr. Thomas Shapter (1849).

In 1955 I prepared an exhibition of works in this library and published a catalogue. Its pages give some idea of the scope of the collections which amount to several thousand volumes. From a fourteenth century manuscript of John of Gaddesden, a Celsus of 1497, and a Galen of the sixteenth century, there are works by John of Vigo, Roger Bacon, Manardus, Eustachius and Vesalius, Harvey, Spigelius, Willis, Glisson, Havers, Musgrave, Burton, Cowper, Bartholin, Paré, Fabricius, Scultetus, Wiseman, Sydenham, Heister, Boerhaave, Haller, Morgagni, Cheselden, Pott, Monro, William and John Hunter, Hewson, Jenner, Abernethy, Astley Cooper, Charles Bell: these are a few of the important names.

I believe this sketch of hospital evolution in Exeter is of more than parochial importance. Hospitals in Exeter were in the forefront of advance; and developments were guided by men of vision who were determined to do something better for medical education than already existed, and furthermore to advance the welfare and maintain the professional competence of practitioners. The long tradition of medical teaching at Exeter is very much alive to-day. My belief is that we owe the stimulus for this in no small degree to the influence of John Sheldon, F.R.S., who died exactly one hundred and fifty years ago in October 1808.

It is a pleasure to acknowledge my great debt to Mr. W. R. LeFanu and Miss Jessie Dobson of the Royal College of Surgeons and to the Librarians of the Royal Society of Medicine and the Royal Aeronautical Society; to Mr. N. S. E. Pugsley, the librarian and keeper of the City Archives, Exeter; Mr. John Lloyd, the librarian of the Exeter Cathedral Library and Miss M. Crichton, its former librarian, Mr. Arthur Rocyn-Jones, Miss B. Farrington, Miss Blanche Patch, Mr. J. Sullivan, the Secretary of the Royal Devon and Exeter Hospital, and Mr. T. Crook, the Secretary of the Exeter and Mid-Devon Hospitals Management Committee; and to the Editor of the *Journal of Bone and Joint Surgery* for permission to quote from Mr. Rocyn-Jones' article on John Haddy James.

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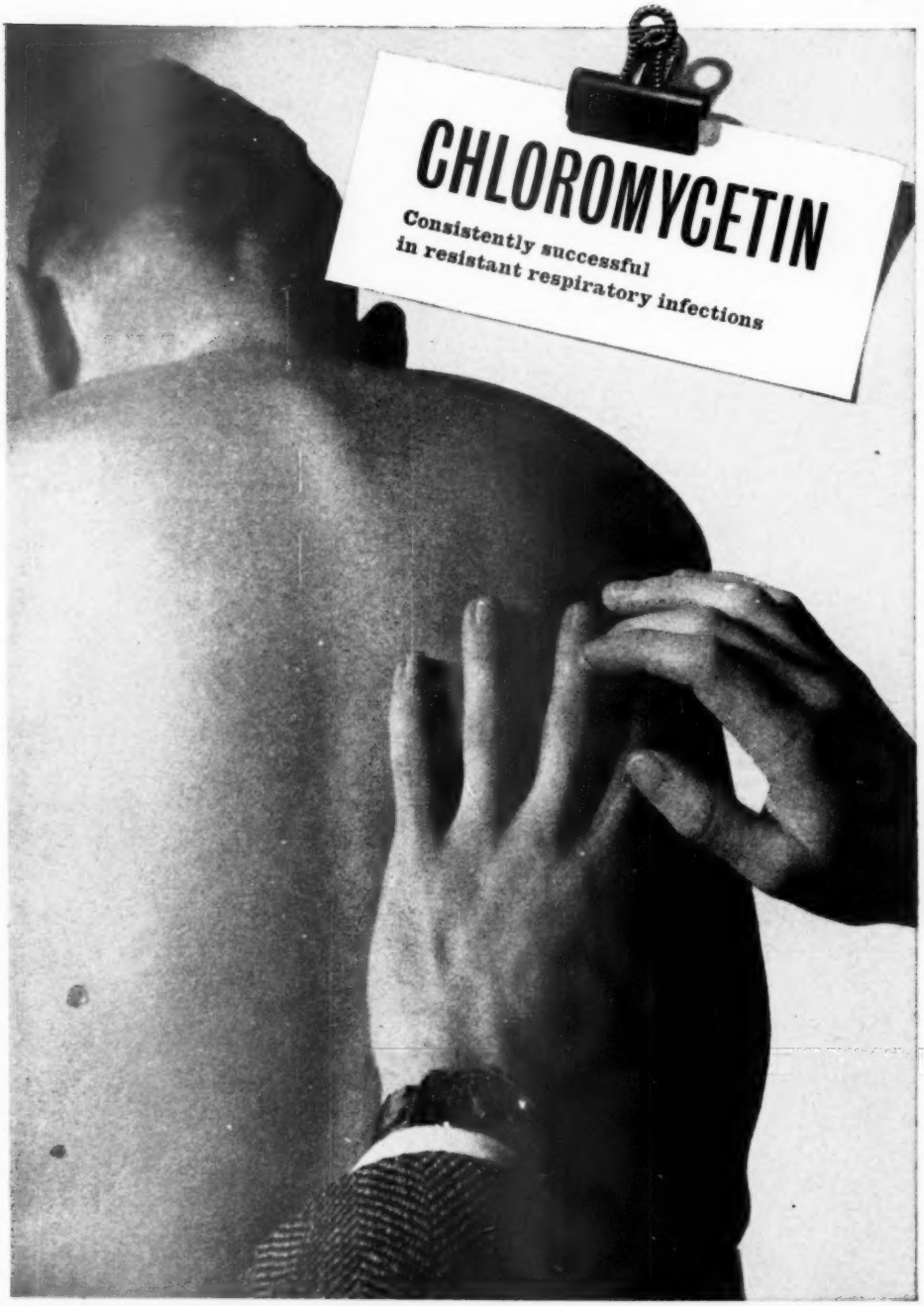

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Section of Anæsthetics

President—H. J. V. MORTON, M.D.

Meeting
October 3, 1958

Dr. H. J. V. MORTON delivered his Presidential Address entitled **Demonstration and Deception by Diagram.**

The Address will be reported in the *British Journal of Anæsthesia.*

Meeting
January 2, 1959

Anæsthesia for Major Disasters

By Group Captain R. L. SOPER, F.F.A.R.C.S.
Royal Air Force

IN the event of hostilities breaking out against these Islands, it is possible that the first we should know about it would be the explosion of atomic or thermonuclear devices over several of our largest cities. This would lead to an enormous number of casualties, far exceeding anything seen before.

The destruction of cities would mean the destruction of many hospitals and their staffs. Many anæsthetists would perish and there would be a grave shortage of apparatus and agents. No replacements would be available for a long time.

Who will give the anæsthetics for these casualties? What will they give and how? What drugs and apparatus are we to recommend for stockpiling?

As I see it, the problem can be divided into three parts:

(1) The role of the remaining specialist anæsthetists.
(2) The selection, training and limitations of the emergency anæsthetist.
(3) Method to be used by the emergency anæsthetist.

The Specialist Anæsthetist

It seems reasonable to suppose that in a national emergency, such as that envisaged above, most available specialist anæsthetists would be employed at major surgical centres (i.e. centres where major surgery is performed) remote from the casualty areas. The work would not be greatly different in type from that of the anæsthetist in a large casualty hospital in the last war. He would presumably have access to all the armentarium remaining available. Some might act as supervisors of, and advisers to, the emergency anæsthetists, and perhaps perform the duties of a sort of super resuscitation officer.

I am not concerned with what the specialist anæsthetist does when the bomb has dropped but with what he should be doing now to prepare for that eventuality.

The advance in anæsthetics in the past twenty-five years has been as outstanding as any other advance in medicine over the same period. There has, however, been a price to pay. The increase in knowledge and complexity of techniques has had the effect of making the subject very much the province of the specialist. The teaching of practical anæsthetics to the student has become more and more difficult because surgeons have come to expect a higher standard of anæsthetics at all times than can be expected of a tyro. The general practitioner anæsthetist has become a *rara avis*. The result of all this is that, except for the specialized few, more and more medical practitioners are becoming unwilling or unable to give a simple anæsthetic. Medical litigation and the observations of coroners after certain fatalities have contributed to the desire not to dabble in anæsthetics.

Something will have to be done about this. A reserve of what I have called emergency anæsthetists must be made available. In the first place I suggest that recruits should be sought amongst practitioners in less densely populated areas. There are many country doctors who still give anæsthetics in their local hospitals. Every encouragement and assistance should be given to these and others willing to be taught the methods suggested for use in national emergency. It may be considered necessary to train nurses and orderlies to give anæsthetics, preferably under supervision.

The specialist anæsthetist must formulate a policy and undertake training.

The Emergency Anæsthetist

If such an emergency ever arises, everyone with any medical knowledge will be required to assist in some capacity or other. In my opinion those selected for training as emergency anæsthetists should live remote from major cities. If sufficient candidates for training are not available from those medically qualified, serious consideration will have to be given to the advisability of training nurses for anæsthetic work. In spite of all prejudice it must be admitted that the nurse anæsthetists employed in the U.S.A. serve a very useful purpose, and surely no one can argue against their employment if there are not enough medically qualified anæsthetists available. Another source of potential anæsthetic skill is among dental surgeons.

Training should consist of a minimum of lectures and a maximum of practical work, using the techniques that will be employed in the emergency. Ample opportunity should be given for the trainee to keep in practice and gain in skill. The scope of the training will of course depend on the calibre of the trainee. The doctor could well be expected to pass a tube and should be able to assess the condition of his patient; and perhaps be able to use more than one technique. The nurse should be able to assess the depth of anæsthesia, be completely familiar with the technique she has been taught and the apparatus employed, take blood pressure readings, set up a transfusion, and give an intravenous injection. In selected cases it should be possible to teach her how to pass an endotracheal tube.

Method

I now come to what I consider to be the most difficult part of my subject: what to use. There can of course be no question of employing the more complicated methods, making use of a mixture of drugs administered by inhalation and intravenous routes, to which we have all grown accustomed in recent years. Spinal analgesia is similarly ruled out; it is in any case not universally applicable. Local and regional analgesia might possibly be employed in selected cases and would probably be carried out by the surgeons. Difficulties are envisaged in obtaining the necessary degree of sterility of solution, apparatus and area under the conditions prevailing, also the process is time-consuming. Intravenous methods at first sight present an attractive possibility but one recalls tragic experience at Pearl Harbour during the last war using a barbiturate.

As has been said: "It must be stressed in the strongest terms that this is not a technique to be used by inexperienced beginners. Intravenous therapy is extremely easy to administer, but just as difficult to control, and such a technique requires the 100% concentration of the anæsthetist . . . and the ability to recognize any toxic signs."

Lignocaine given by the intravenous route has attracted considerable notice recently but the warning quoted above appears in an article dealing with this subject (De Clive-Lowe *et al.*, 1958).

Hayward-Butt (1957) describes a state in which the patient remains conscious but free from fear and pain, induced by the injection of a mixture of drugs. He has named this condition ataralgesia. I have no experience of this procedure and according to his published figures the results are not always satisfactory and have to be supplemented with an intravenous barbiturate. I feel this is not the technique for the emergency anæsthetist at present, but one worth keeping in mind for future development.

If we dismiss hypnotism (good, but effective even in the hands of the expert in only a percentage of cases, and very time-consuming) we are left with the inhalation anæsthetics. It is in this direction that I think at present our choice must lie.

The gaseous anæsthetics have much to commend them; but they are difficult to handle and store, both on account of the weight and bulk of their containers and their evanescent nature. They require somewhat elaborate apparatus for their metering and administration.

We are left with the volatile agents: chloroform, trichlorethylene, ethyl ether and halothane. The rarer ethers will not be discussed.

Chloroform is non-inflammable and very potent—a little goes a long way: both very important characteristics for our purpose. The safety margin is, however, narrow and Waters (1951) has shown in his reassessment of the drug that it must be considered as more dangerous than others in use. Given in apparatus designed to keep its concentration constant, it might have a role in a future war as it had in the last when it was adopted by Macintosh for use in new apparatus designed to be used by medical officers dropped with paratroops.

Halothane has the advantages of chloroform and the additional one of being safe. It requires a dosimetric vaporizer for our purpose and I do not know of one specifically designed for use with this drug, which is independent of a supply of compressed gases for its operation. The drug is at present extremely costly and one wonders if it could be made in sufficient quantities to meet the requirement. It is, however, a most attractive agent and research with it with this use in mind would be well worth while.

Trichlorethylene can be used in a dosimetric inhaler to produce full anæsthesia. I used it in this way during the last war. Recovery, however, tends to be very prolonged. There is in existence a large number of inhalers for this drug designed for producing analgesia for midwifery. These are dispersed throughout the country and could well be used to produce relief from pain for minor surgical procedures. Trichlorethylene is also manufactured on a very large scale for commercial purposes. It should therefore be fairly easily obtainable, even under the conditions envisaged. Perhaps we should pay more attention to the possibilities of trichlorethylene.

There remains ethyl ether. In spite of its inflammability and irritant properties, it is extremely safe. That is, there is a wide margin between satisfactory anæsthesia and a lethal overdose.

During the last war Macintosh and his coworkers showed what could be done with ether used in a properly designed dosimetric vaporizer. The Oxford vaporizer (Macintosh and Mendelssohn, 1941) was used widely by the Services under active conditions and enabled an anæsthetist to be in charge of four or more patients at the same time.

The original Oxford vaporizer is no longer obtainable but it has been succeeded by a new one (Epstein and Macintosh, 1956) from the same stables. I have myself designed one, less perfect in its control of concentration perhaps, but simple and robust, and I feel, accurate enough to meet our requirements.

The desiderata of such an apparatus are:

(1) Reasonably constant output.

(2) Ability to operate using atmospheric air as the vaporizing agent.

(3) Provision of a means of artificially ventilating the lungs.

(4) Portability (preferably with one hand).

(5) Robustness.

(6) Good shelf life.

It is especially important with apparatus of this type that the face-piece should be a good fit, otherwise it may not be possible to obtain sufficient concentration of the drug to ensure anæsthesia. Bearing in mind the long storage such apparatus will, we hope, have to survive, those which depend on a pneumatic cushion for their air tightness would be better avoided. Development of a non-perishable face-mask would be of great value.

Ancillary equipment presents no insuperable problem. Rubber should be avoided where possible and replaced by plastic (breathing tube bellows—but not breathing bag—Magill tubes, &c.) or metal (airways). It will of course be necessary for all equipment to be properly packed and stored and to receive periodic inspection, when defective items can be replaced. One item which immediately comes to mind is the laryngoscope battery, although modern batteries if properly prepacked have a very fair shelf life.

Only a few weeks ago I was told of a demonstration of a casualty centre planned for such an emergency as has been here considered. Lifelike mock-ups of injuries were shown and surgical procedures were discussed in some detail. Anæsthetics? Oh, either a medical officer or an auxiliary will give them. The method? A bottle of ether represented the anæsthetist's equipment.

Papers are written and plans are made for the handling of casualties in the next war, but hardly a word is heard about anæsthetics. Let us make our plans. It is later than you think.

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Discussion

Colonel K. F. Stephens, R.A.M.C.:

The Likely Role of the Anæsthetist and of Anæsthesia in the Early Surgical Treatment of Mass Casualties

The Army Medical Services in recent years have devoted considerable attention to the study of problems associated with the management of mass casualties, not only as applied to military situations affecting troops in the field, but also in connexion with the Army's secondary role of providing aid to the Civil Power under conditions of national emergency.

In 1956 the Royal Army Medical Corps was asked by the Home Office to demonstrate the type of assistance which the Army could provide under these circumstances. As a result of the subsequent study of the problems involved, certain principles governing the evacuation and treatment of mass casualties were established.

It became obvious that in order to prevent hospitals on the periphery of the disaster area from being overwhelmed by enormous numbers of patients, many of whom might not require hospital treatment at all, some system of casualty

sorting is essential, applied well forward of the hospital area. It was planned therefore to provide "filter units" at the periphery of the disaster area, now termed Forward Medical Aid Units by Civil Defence, where this vital process of casualty sorting could be carried out.

At this "filter unit" level casualties, after preliminary monitoring and cleansing, are grouped into four main categories:

(1) Minor treatment (not requiring hospitalization).

(2) Expectant treatment (unfit to be moved and unlikely to survive).

(3) Delayed treatment (fit for transport to hospital).

(4) Immediate treatment.

Those selected for immediate treatment will require a variety of short major surgical operations, and it is to the problem of providing anæsthesia for these operations that attention is particularly directed.

Examples of the type of operations envisaged at this level are the control of hæmorrhage, closure of sucking wounds of chest, toilet, closure and fixation of compound fractures, completion of partial traumatic amputations, tracheostomy, &c. All, in fact, short life-saving procedures designed to render the patient transportable for more definitive treatment at hospital level.

Time will prove to be a limiting factor. An estimate that 1,200 casualties per twenty-four hours at "filter unit" level may be the number requiring immediate treatment following the explosion of a 10-megaton bomb on a densely populated area has been given by Ahern (1957). Assuming the availability of 10 surgical teams, this allows an average of approximately *ten minutes only for the treatment of each case*.

It should be remembered that operating conditions will be improvised in every sense of the word, drugs (including medical gases) and equipment will be in short supply, and skilled assistants will not be available. The patients will be suffering from varying degrees of oligæmic shock, for adequate resuscitation at this stage is likely to be quite impracticable and the best that can be expected is some restoration of blood volume with plasma or plasma substitutes.

In brief, the problem is to provide anæsthesia for life-saving operations of short duration on severely shocked patients. Speed of induction and rapid recovery of consciousness are essential factors. Simplicity and safety are vital, as the administration is likely to be left in unskilled hands.

Cyclopropane

To meet the role of the Forward Medical Aid Unit the Army has available the Field Ambulance, a well-tried Medical Unit eminently suited to this work. The anæsthetic equipment provided for such a Unit comprises at the present time a full-scale set of modern anæsthetic apparatus, instruments and drugs for each surgical team, and also includes E.M.O. ether/air inhalers and of course Schimmelbusch masks with ample supplies of ether and chloroform.

I venture to suggest that, in the light of the special conditions governing the anæsthesia of mass casualties at this level, as outlined above, this range of equipment, however desirable under more normal conditions, may prove inadequate to the task. It seems that consideration should be given to some simple inhalational method capable of producing safe surgical anæsthesia of short duration, which can be administered by unskilled assistants after a minimum of training and with a minimum of supervision.

Surely cyclopropane has much to recommend it in this capacity.

It is several years now since Bourne (1958) designed a portable single-dose anæsthetic apparatus for the administration of cyclopropane, nitrogen and oxygen in known proportions. Bourne's intention was for his apparatus to be used for the anæsthesia of patients in the dental chair and in the hospital out-patient department during minor operations not exceeding one and a half to two minutes in duration. Hingson (1954) has shown that the addition of a small soda-lime canister for carbon dioxide absorption to this type of apparatus enables the anæsthesia to be prolonged for ten to fifteen minutes without refilling the bag and without depriving the patient of oxygen. This has been confirmed recently by Mushin and Thompson (1958), who have reported favourably on their clinical experience with the use of Hingson's apparatus for the anæsthesia of over 100 patients. Both Bourne and Hingson claim that the proportions of cyclopropane, oxygen and diluent gas (nitrogen or helium), with which their apparatus is charged, do not constitute an explosive mixture.

This method of administering cyclopropane is simple, safe and effective and can be easily mastered by the uninitiated. The apparatus is compact, inexpensive and highly portable. I suggest therefore that in the use of cyclopropane with this type of single-dose apparatus lies a most suitable method for the anæsthesia of shocked exsanguinated casualties for surgical operations of short duration.

A plea is made for the development and production of apparatus for this purpose now, for,

in addition to meeting this special requirement for mass casualties, there seems little doubt that a wide use would be found for this simple and inexpensive equipment for providing short anæsthesia for minor operations on ambulatory patients in normal peacetime practice.

Halothane

Halothane has many attractive features in just this role and very compact apparatus for the precise and economic administration of halothane in oxygen has been devised recently by Burton (1958) and is in fact in the course of final clinical trial at the present time.

The overall safety of halothane for the anæsthesia of *inadequately resuscitated casualties* is, however, open to question, and further research is necessary before an opinion can be formed as to the suitability of this agent for anæsthesia for the type of work undertaken at "filter unit" level.

Conclusion

It is important to formulate as soon as possible a definite policy governing the drugs and equipment required for the mass anæsthesia of casualties following a major disaster. Without such a policy it is unlikely that adequate provision for anæsthesia will be made, and the training of doctors, nurses and others to administer anæsthetics in such an emergency may be misdirected.

The possibility of a nuclear explosion with subsequent unprecedented numbers of casualties cannot be disregarded. We must be ready for such an eventuality.

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Dr. Philip H. Moore (London):

In the event of war being declared by the simultaneous explosion of a number of thermonuclear weapons on strategic targets in this country, anæsthetists will be able to help in the work of resuscitation. Some consideration should be given to the use of chlorpromazine, pethidine and promethazine in varying proportions, possibly coupled with cooling, in the treatment of shocked patients. Relief from pain and apprehension would be produced, surgery being possible under this alone or with minimal amounts of local or general anæsthesia. These are potent drugs and their use should be supervised by a specialist anæsthetist.

Anæsthetic Personnel

We can only guess what the conditions will be following an attack such as we have considered. They would depend on the number of targets attacked, on the spacing of the bombs throughout the country and on the position of the large hospitals in relation to them.

Assuming the destruction of London, peripheral hospitals, with a high proportion of London consultants on their staffs, might well find themselves with depleted anæsthetic departments, though I would venture to suggest that there would be sufficient resident anæsthetists to carry out the work required. In the provinces, casualties would be taken to hospitals available in the nearest unaffected area, where, in all probability, the consultant staff would live reasonably near the hospital, and so survive.

Nevertheless, there is bound to be a shortage of trained anæsthetists. I agree that general practitioners, particularly in less populated areas, are a potential source, but general practice is one of the most overworked branches of medicine, and I doubt if the general practitioner would have the time to spare, not just to attend a course, but to keep in practice. Dentists could be used if they were willing to be trained and both medical and dental students would consitute an additional source of supply.

In this country nurses are not trained to give anæsthetics. If we are going to ask them to do so, we shall have to add considerably to their curriculum and, of course, obtain the approval and help of the General Nursing Council. The shortage of nurses in general must be remembered, and the fact that in the situation under discussion they may already be fully occupied as nurses and unable to be spared as anæsthetists.

Lastly we must consider the desirability of submitting our patients, for training purposes, to the more primitive techniques and agents which would be required, and also to the attentions of the relatively unskilled administrator. It would undoubtedly lower the high standard of anæsthesia which the public can rightly expect in this day and age.

Our first approach should be to the medical students. They watch the complicated present-day techniques with interest and come away impressed by what they have seen, forbidden to do likewise and unable to do anything else. The teaching hospitals should make sure that they are turning out doctors who have a sound knowledge of simple techniques in anæsthesia. Secondly, junior medical officers should be encouraged to give some anæsthetics. Casualty officers have excellent opportunities and house surgeons and

physicians should be spared from their other duties to give simple anæsthetics in the operating theatres. Surgeons should familiarize themselves with existing apparatus so that they could direct an untrained anæsthetist, while still carrying on with their own work.

Hospitals should welcome general practitioners and dentists, who are willing to attend, and allow them to give anæsthetics.

Drugs

We must assume that supplies of compressed gases will soon run out and replacements will be unobtainable. This leaves us with local techniques, spinal and epidural analgesia, all of which can be given by the surgeon in the absence of a trained anæsthetist. We are also left with the volatile anæsthetics, ether, chloroform, trichlorethylene, halothane, ethyl chloride and divinyl ether. I would rule out halothane because of the cost of stock-piling and the risks of its use in untrained hands, and divinyl ether because of the difficulties of storage due to its extreme volatility. Ethyl chloride could be used for induction in the absence of an intravenous barbiturate. I agree with Group Captain Soper over the dangers of using intravenous drugs, but I feel that if a limit to the amount of thiopentone was imposed, say 250 mg., it would be reasonably safe as an induction agent.

With regard to the first three, ether has proved to be the safest by far, particularly in unskilled hands. Trichlorethylene would be of value for surgery requiring first-plane anæsthesia and for analgesia in minor procedures. It is possible that chloroform would come back into the picture. We must ask ourselves if it is justifiable to teach junior anæsthetists and students to use this potent and dangerous drug.

Apparatus

Under emergency conditions, open mask techniques would have to be used or, where available, draw-over machines of the type described by Group Captain Soper. In undamaged hospitals, where complete anæsthetic machines are available, I would suggest that the circle absorption unit can be modified to act as a draw-over vaporizer. The Marrett apparatus already incorporates the means to vaporize ether with atmospheric air, and other circle absorbers can be converted with the greatest of ease. I have used one of these machines in this way to produce ether-air anæsthesia for abdominal surgery.

Dr. J. G. Bourne (London and Salisbury):

If nuclear war came, the need would be for simple apparatus; and I have reason for thinking that the best anæsthetic would be cyclopropane.

I agree with Colonel Stephens that the problem is to get a few minutes' quiet anæsthesia, with rapid induction and recovery, and by a method that could safely be used by anæsthetists of limited experience. Now, speed of induction and recovery is governed by an anæsthetic's solubility in blood (Henderson and Haggard, 1927; Kety, 1950, 1951; Bourne, 1957). Low blood-solubility favours rapid induction and recovery, whereas with anæsthetics of high blood-solubility, like trichlorethylene or ether, induction and recovery are slow. We should therefore select an anæsthetic of low blood-solubility. The blood-solubilities of the different anæsthetics, in terms of Ostwald solubility (or partition) coefficients, are as follows:

Cyclopropane	0·46
Nitrous oxide	0·47
Divinyl ether (Vinesthene) ..	2·0*
Ethyl chloride	2·0
Halothane	3·6
Chloroform	7·3
Trichlorethylene (Trilene) ..	9·0
Diethyl ether (ether)	15·0

*The blood-solubility of divinyl ether has never been measured; the value given is a rough approximation suggested by its solubility in water.

It will be seen that cyclopropane is the least soluble, and therefore the most flexible, of all the inhalational anæsthetics. In this respect, therefore, cyclopropane comes out best.

Blood-solubility, however, has wider implications. For, because it determines (inversely) the extent to which tissue tension keeps pace with alterations in inspired tension, blood-solubility influences an anæsthetic's safety. With an anæsthetic of low blood-solubility, increase in tissue tension follows hard on the heels of increase in inspired tension. If an anæsthetic of low blood-solubility happens also to be very potent, a gross overdose might easily be given and result in lethal tissue tensions within a few breaths. This is why ethyl chloride is so dangerous. Its power is such that it is probably effective at concentrations as low as 1% or 2%. Its volatility and usual mode of administration allow it to be given inadvertently at 30 or more times this amount. As a result of its low blood-solubility, tension in the brain and heart would quickly reach a considerable fraction of this huge overdose. With cyclopropane, no such gross overdose is possible. For, contrary to what is commonly believed, cyclopropane is not very potent. Its anæsthetic range runs up to concentrations higher than 30%, so that at the worst it could be given at only three times a therapeutic amount. To be safe, therefore, an

anæsthetic of low blood-solubility should not be too potent. In this respect also cyclopropane shows up favourably.

Halothane is just as potent as ethyl chloride; and though it is less volatile and more soluble than ethyl chloride, it needs complex apparatus if a dangerous overdose is to be avoided. Moreover, its greater solubility makes it less flexible than cyclopropane. Divinyl ether might give good results; but its potency is not much less than that of ethyl chloride and no dosimetric method of administering it has been devised. Nitrous oxide is too weak. And so we come back to cyclopropane.

When cyclopropane is given at a constant inspired concentration of 50%, anæsthesia is established within a minute; after about three minutes, anæsthesia is deep enough for intubation; and after four or five minutes, respiration peters out. If, however, a 6-litre bag is charged with 50% cyclopropane (and 50% oxygen) and the patient then breathes in and out of the bag, only the first breath contains cyclopropane at a concentration of 50%. Subsequent breaths become progressively diluted with air from the lungs down to a certain point. Such an arrangement gives a wide margin of safety in brief administrations for dental extraction, which was what I had in mind when I originally described and recommended this method (Bourne, 1951, 1952, and 1954). Later, I used 50% cyclopropane with 25% oxygen and 25% nitrogen, which is non-ignitable (Bourne and Morton, 1955). The bag can be filled with this mixture from a pair of Sparklet bulbs, discharged by a special "gun" (Bourne, 1958). However, the gun could be dispensed with and an ordinary soda-siphon charging key used instead. We would then have the simplest and cheapest apparatus imaginable; and with it we could charge the bag with any mixture of the three gases we chose to put in the bulbs. Loaded bulbs could be stock-piled with the ammunition of war.

For the longer administrations that we are considering here, a soda-lime canister would have to be added; and Hingson's (1958) mixture, consisting of 40% cyclopropane, 30% oxygen (and 30% nitrogen), which is also non-ignitable, would be more suitable than mine. With it, overdose would be impossible, no matter how long the administration was continued; but in my opinion the oxygen would begin to run short within ten minutes. If the operation lasted longer than this, it would be simple to recharge the bag, allow the patient to breathe air for two minutes (when anæsthesia would show signs of becoming light) and then re-apply the mask and continue as before. This could be repeated as often as necessary and therefore operations of any length could be catered for.

I am satisfied that, with both Hingson's mixture and mine, the danger of explosion is eliminated, and the risk of fire reduced to negligible proportions. I consider that cyclopropane, used in this way, is uniquely suitable, not only for war casualties, but also for the millions of out-patients anæsthetized each year in this country. I am supported in this view by my own experience in 3,000 cases and by that of Hingson in 10,000 cases (Hingson *et al.*, 1958).

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Dr. Ronald Woolmer said it seemed to him that in the circumstances envisaged they would have to confine themselves to the simplest possible method. To him, that meant "rag and bottle" with ether as the main volatile agent. A possible subsidiary volatile agent, which had not been mentioned but which might be considered at least for induction, was a constant-boiling mixture of halothane and di-ethyl ether. He had had no experience of this mixture, but would be interested to hear about it from others. Those who advocated intravenous methods should remember that stocks of glass syringes, and glass ampoules, might have been shattered by the explosion. Volatile liquids could be kept in tins or plastic bottles.

Mr. C. Langton Hewer, referring to Dr. Woolmer's suggestion that a halothane-ether mixture might be useful, said that since di-ethyl ether was very much less potent than halothane and was only present in 32 parts in 100 by volume in an azeotropic mixture, it was difficult to see that it could have any effect other than slight dilution of the halothane.

Dr. J. D. Laycock said that during the Burma campaign in 1943–45 he had to deal with large numbers of casualties on many occasions and used thiopentone or hexobarbitone as the sole anæsthetic in 5 cases out of 6. Of the remainder most were penetrating abdominal injuries all of whom were anæsthetized with ether, either by means of Ogston's inhaler or by connecting the endotracheal tube to a short length of rubber tubing which hung loosely inside a wide-necked bottle containing ether.

By these means apparatus was reduced to an abso-

lute minimum and comparatively small amounts of ether were adequate.

The policy with thiopentone was to induce sleep as the dressings were removed and the wounds cleaned but with the minimum depression of reflexes. A restraining strap was put across the thighs and further thiopentone was given in doses only sufficient to prevent such reflex movements as would cause embarrassment to the surgeon.

When dealing with large numbers of casualties insistence on several hours of pre-operative starvation was impracticable. In actual practice no trouble whatever occurred with post-operative vomiting. Reflexes returned rapidly and the immediate post-operative care was left in the hands of very inexperienced orderlies with a minimum of anxiety.

The use of Gordh's needle would be of considerable value here. Dr. Laycock said that if he had to deal now with a large number of cases requiring anæsthesia for minor surgery and very little trained assistance he would put a Gordh needle into each patient, instruct the assistants in keeping an airway, apply a restraining strap to each case and then go from one case to another giving more thiopentone as dictated by the state of their reflex activity.

Dr. A. G. Doughty said that Group Captain Soper had cited the unhappy experiences of the anæsthetists at Pearl Harbour as the main reason for not recommending thiopentone as an agent for use in major disaster anæsthesia. Used with caution and with apparatus for artificial respiration at hand, it combined the advantages over inhalational methods of being rapid in onset and certain in its non-inflammability. The latter property was likely to assume importance under the circumstances envisaged as lighting was more likely to be from paraffin lamps than by electricity.

In view of the impossibility of foreseeing what agents or apparatus would be available to individual anæsthetists working in the disaster area, it seemed important that one should be prepared to practise any of the simpler methods of anæsthesia.

Dr. F. M. Purcell said that in recent years he had had experience in treating emergency injuries of great severity in miners in West Africa; sometimes many cases simultaneously. Relief of pain was the most urgent, by morphia $\frac{1}{4}$ grain to $\frac{1}{2}$ grain. But the general anæsthetic had to be given by a trained African nurse. He had found chloroform on an open mask the best method; ether was unsuitable because it was much too slow and was required in large amounts. The risk of over-dosage with chloroform by a trained nurse was slight but had to be accepted. He suggested that such crude methods were likely to be unacceptable to a body of professional anæsthetists confronted with a vague hypothetical situation; therefore, the decision on the methods to be used in order to anticipate a practical situation would have to be made by a responsible group of doctors.

Professor Sir Robert Macintosh held that it was unjustifiable to deprive present-day patients of the advantages of modern anæsthetics in order to train unqualified anæsthetists to meet an emergency which might never arise.

He pointed out that an E.M.O. inhaler calibrated for halothane was available, and also suggested that the Mitchell needle might have advantages over the Gordh as it was more robust.

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Meeting
December 3, 1958

DISCUSSION ON ASCITES AND ITS MANAGEMENT

Dr. Sheila Sherlock (London):

Mechanisms for the Formation of Ascites

In 1896, Starling postulated that "at any given time, there must be a balance between the hydrostatic pressure of the blood in the capillaries and the osmotic attraction of the blood for the surrounding fluids". This hypothesis was based on the use of peritoneum as a semipermeable membrane allowing the passage of solutes but impervious to colloids. Applying this concept to ascites, the forces keeping the fluid in the capillaries are the serum colloid osmotic pressure and the ascitic fluid pressure and the forces tending to form ascites are the portal capillary pressure and the colloid pressure of the ascitic fluid (Fig. 1). If a patient is neither forming nor absorbing ascites, these positive and negative forces should balance. Our observations on the mechanisms of ascites apply to patients with cirrhosis of the liver and to patients with normal liver structure but with an extrahepatic obstruction to the portal vein. We have not studied patients with malignant ascites in whom increased permeability of the peritoneal membranes assumes greater importance.

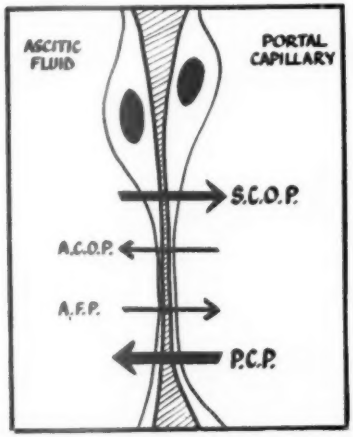

FIG. 1.—The ascitic fluid is separated from the capillary lumen by the peritoneal membrane and the portal capillary wall. The forces keeping fluid in the capillaries are the colloid osmotic pressure of the serum (S.C.O.P.) and the hydrostatic pressure of the ascitic fluid (A.F.P.) The forces tending to form ascites are the portal capillary pressure (P.C.P.) and the colloid osmotic pressure of the ascitic fluid (A.C.O.P.). In a steady state these forces should balance.

We have measured the colloid osmotic pressure of serum and ascitic fluid by the osmometer devised by Rowe and Abrams (1957). The portal capillary pressure is reflected by the pressure in the pulp of the spleen (Atkinson and Sherlock, 1954) and the intra-abdominal pressure can be measured directly. It is therefore possible to measure all four factors in the Starling equation. When the effective portal pressure is plotted against the effective serum colloid osmotic pressure the expected linear relationship according to the Starling hypothesis is not obtained (Cherrick *et al.*, 1959). In particular, patients are seen with a high effective portal pressure but no ascites, or with a portal pressure which is hardly raised but yet showing ascites. The effective serum colloid osmotic pressure seems to provide a better index than the effective portal pressure of whether or not a given patient will show ascites. The dividing line is a serum colloid osmotic pressure of about 270 mm. H_2O. The failure to balance Starling's equation may be due to additional factors not considered. The patients may not be in a stable state, i.e. not forming or absorbing ascites. Lymphatic flow in the thoracic duct is increased in patients with hepatic cirrhosis (Blomstrand, 1958). The osmotic pressure of the interstitial fluid of patients without ascites cannot be measured. Also the peritoneal membrane itself might not be strictly semipermeable but behave in a dynamic fashion.

These observations suggest that elevation of the serum colloid osmotic pressure might be an effective therapeutic measure in ascites. Occasionally a most dramatic diuresis follows large doses (600–1,000 grams as 100 grams intravenously every other day) of salt-poor human albumin. The treatment, however, is expensive and occasionally complicated by hæmorrhage from œsophageal varices. In successful cases, the gradient between serum and ascitic colloid osmotic pressure is increased and a diuresis of water and sodium follows. The albumin might also act by expanding the plasma volume and so diminishing the increased aldosterone production (Bartter, 1958) with consequent loss of sodium

and water in the urine. This treatment, however, is not always successful and the reasons for failure are not clear.

The importance of portal hypertension is emphasized by end-to-side porta-caval anastomosis being occasionally successful in the rare cirrhotic patient with "stable" ascites and a virtually normal serum albumin (Eisenmenger and Nickel, 1956). Such operations are usually followed by gross peripheral œdema. This is expected for the hypo-albinæmia persists or develops, and when portal pressure is lowered the fluid will accumulate in peripheral parts where venous pressure is high. Recently McDermott (1958) has suggested the use of a double end-to-side porta-caval shunt, both ends of the portal vein being implanted separately into the inferior vena cava. Side-to-side porta-caval anastomosis would have a similar effect. This relieves portal hypertension and further effects a hepatic decompression. This operation is based on the premise that ascites can be produced by any procedure that obstructs the outflow from the liver but not by measures designed to obstruct the portal vein. The ascites in "experimental outflow block" is believed to be due to increased transudation of hepatic lymph. Such a passage has never been proved in man but this remains an interesting speculation.

The operation of ileo-entectropy (segmental eversion of the ileum) was devised to evaluate the absorptive function of intestinal mucosa for the control of ascites (Neumann *et al.*, 1957). This operation may act as a variant of the Talma-Morison omentopexy, simply encouraging a collateral circulation, or the fluid may be absorbed through the mucosa into lymphatic channels. Certainly the operation is not successful unless the ileal mucosa is present and the serosa of the ileal segment is sutured to the abdominal wall.

The combination of an elevated portal venous pressure and a low plasma osmotic pressure results in fluid passing into the peritoneal cavity. The contraction of the extracellular and plasma volume is a stimulus for the adrenal to secrete aldosterone and so maintain isotonicity of the extracellular fluids. Increased amounts of aldosterone have been found in the urine of patients with cirrhosis forming ascites (Wolff *et al.*, 1956) and the very low urinary sodium output with low sodium-potassium ratio are compatible with this increase. Surgical adrenalectomy has been used in an attempt to reduce the effect of this excess aldosterone (Marson, 1954; Werk *et al.*, 1957). Amphenone, a substance which antagonizes the production of several adrenal hormones, has been used but is too scarce and toxic to have widespread application (Summerskill and Crabbé, 1957; Wolfe *et al.*, 1957). Recently some steroidal-17-spirolactones have been synthesized which have some anti-aldosterone activity in experimental animals (Cella and Kagawa, 1957). Observations in man suggest that these substances act as peripheral inhibitors of aldosterone and do not affect the production of aldosterone or other hormones by the adrenals. The more active, SC 8109, produces a sodium and water diuresis in some patients with cirrhosis and intractable ascites (Kerr *et al.*, 1958) (Fig. 2). The preparation in sesame oil for intramuscular use may even

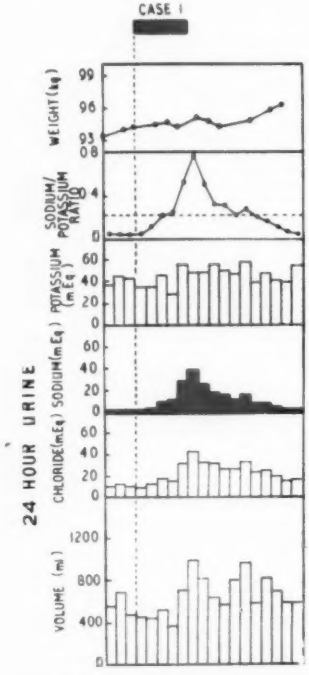

FIG. 2.—A microcrystalline preparation of SC 8109 given intramuscularly to a patient with ascites complicating cirrhosis of the liver results in an increased urinary sodium excretion and a rise in the urinary sodium : potassium ratio. Potassium excretion is unchanged and body weight does not fall.

[Reproduced from Kerr *et al.* (1958) by kind permission.]

produce clinical weight loss and relief of œdema and ascites. SC 8109 gives promise of being a valuable drug in the treatment of difficult cases of ascites. Unfortunately synthesis of the compound is tedious and costly and has not yet been undertaken on a commercial scale.

Although sodium retention is probably not a primary factor in the production of ascites, dietary sodium restriction will control the

accumulation of fluid. The diet must be a very rigid one (less than 20 mEq. sodium per day) and continued for many months. It can be supplemented by diuretics. The most active seems to be chlorothiazide, although even this potent diuretic may fail to have any effect on sodium excretion in patients who are retaining sodium very avidly (daily urinary excretion less than 1 mEq.) (Read *et al.*, 1958). In patients with liver disease having a diuresis following chlorothiazide the concomitant enormous loss of potassium is associated with hypokalæmia; this seems to precipitate hepatic coma (Sherlock *et al.*, 1958). In such patients chlorothiazide must be supplemented by large potassium supplements and even 200 mEq. daily may be insufficient to prevent hypokalæmia. Atkinson (1958) has recently demonstrated that chlorothiazide lowers portal venous pressure. It remains to determine whether this is a primary effect or secondary to the diuresis.

Increased antidiuretic hormone activity, whether over-production or failure of hepatic destruction, remains a possibility. Lee and Bissett (1958), using a reliable method, have shown increased amounts of antidiuretic hormone in the jugular vein blood and urine of patients with cirrhosis who are forming ascites.

Although control of fluid retention may often be achieved by medical or surgical means, this does not provide the patient with a new liver. Death from other complications of chronic liver disease is therefore frequent (Table I). In a certain proportion of patients, ascites is uncontrolled and death rapidly supervenes. These patients show other features of liver failure such as neuropsychiatric changes and jaundice, and have a very low serum sodium level (Hecker and Sherlock, 1956). In such circumstances it is difficult to envisage dramatically good results from any currently available surgical or medical procedure.

TABLE I.—MEDICAL TREATMENT OF 75 PATIENTS WITH CIRRHOSIS COMPLICATED BY ASCITES

Control of Ascites Does Not Prevent the Other Complications of Chronic Liver Disease

Response of ascites	No.	Died		
		Hæmorrhage ± coma	Liver cancer	Other
Disappeared ..	19	1	2	0
Controlled ..	32	16	1	3
Uncontrolled ..	24	18	6	0

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Mr. Peter Knipe for **Mr. Alan Hunt** (London):

Results of Treatment from Porta-caval Anastomosis, Lieno-renal Anastomosis and Hepatic Artery Ligation

From Mr. Hunt's series of cases of portal hypertension (over 350 to date) two large groups of cases emerge, the extra- and the intra-hepatic obstructions. The intra-hepatic group has been divided into the mild, moderate, and severe cirrhotics, and there are 262 patients in the two latter groups and 117 shunt operations. Ascites is an indication of severe liver damage, being thereby absent from the mild group. It is common in the other two groups either primarily or following hæmorrhage; of the 262 patients, 47 had ascites at the actual moment of shunt or hepatic artery ligation, and these form the basis of this paper.

Two things should be stressed at the outset. First, surgery is complementary to medical treatment and not a competitor. Before these patients can be offered a shunt, they must be given intensive medical treatment, often for three months or more. Our hope is that liver function will improve, the serum albumin rising to at least 3·2 grams/100 ml., with corresponding improvement in their general state. The majority will lose their ascites on this regime and do not therefore come into this report. Secondly, only 117 shunts have been done on this group of 262 patients (approximately 45%). The other 55% per cent have not been fit enough for this procedure. They have died before operation, in

spite of operation to arrest hæmorrhage, or of liver failure; many have had other smaller procedures as a direct attack on the ascites. Serum albumin of less than 3·2 grams/100 ml. was (except for one case) a contra-indication to shunt, but ascites alone was not. 11 patients had a hepatic artery ligation with serum albumin levels of under 3·2 grams/100 ml. and all died.

Operations Available

49 operations have been done to influence ascites on 47 patients. For this report we have excluded operations attacking portal-systemic anastomoses as they do not affect ascites, and operations promoting anastomoses, such as the Talma-Morison, as we feel they are of no permanent value.

(1) *Hepatic artery ligation* (Table I).—14 patients were submitted to this operation in the early years of this series; only 5 survived, and in 2 of these the ascites was unaffected. The 11 who either died or whose ascites was unaffected all had a serum albumin of under 3·2 grams/100 ml. In spite of the most intensive medical treatment their response was thus nil and surgery a despairing hope. To-day they would have been rejected. Only 3 had levels over 3·2 grams/100 ml. and to-day they would have been shunted. One died later of hæmorrhage and 2 are still alive and well. From these facts we suggest that a serum albumin of under 3·2 grams/100 ml. is a contra-indication to definitive surgery, and that hepatic artery ligation is not of value, more particularly in the presence of varices.

(2) *Porta-caval anastomosis* (Table II).—24 patients had a porta-caval anastomosis with 5 deaths. One case thrombosed her shunt, later dying with her ascites worse. Of the 3 late deaths 2 returned to work ascites-free for one and two years before liver failure supervened. The third, a dypsomaniac, continued to drink with an ascites-free belly until after a year he died with ascites, anasarca and liver failure. 15 may be termed successes, 3 dying from other causes, ascites-free to death, and the other 12 being still free from ascites and at work between one and five years post-operatively.

(3) *Lieno-renal anastomosis* (Table III).—8 patients had a lieno-renal shunt and 7 survived.

Table III.—Lieno-renal Anastomosis

		%
Cases	8	
Operative deaths	1	(12·5)
Liver failure		
Successes	7	(87·5%)
Surviving	6	
Carcinoma of bronchus at 30/12	1	
	8	

All these are considered successes, one dying ascites-free from carcinoma of the bronchus after two and a half years, the others being well up to six years. It is of interest to note how very dramatic and sudden is the response of ascites to shunting (*see* Fig. 1).

These three operations comprise all but one in this series of 47. The other operation was an ileo-entectropy which is recorded separately.

During the course of cirrhosis, ascites may develop either insidiously or acutely. We have defined ascites in this paper as ascites at the time of operation. This definition thus excludes those patients whose ascites disappeared with medical treatment. Ascitic patients are generally thought

Table I.—Hepatic Artery Ligation

			%
Cases		14	
Operative deaths		9	(64·3)
Hæmorrhage	1		
Heart failure	1		
Liver failure	7		
Late deaths		3	(21·4)
Hæmorrhage—no ascites	1		
Liver failure—ascites	2		
Successes		2	(14·3)
		14	

Table II.—Porta-caval Anastomosis

			%
Cases		24	
Operative deaths		5	(20·8)
Liver failure	4		
Pericarditis	1		
Late deaths		3	(16·6)
Liver failure + ascites	1		
Liver failure—no ascites	2		
Thrombosed shunt		1	
Successes		15	(62·5)
Surviving	12		
Dead—Carcinoma of bronchus	1		
Carcinoma of liver	1		
Perforated duodenal ulcer	1		
	3		
		24	

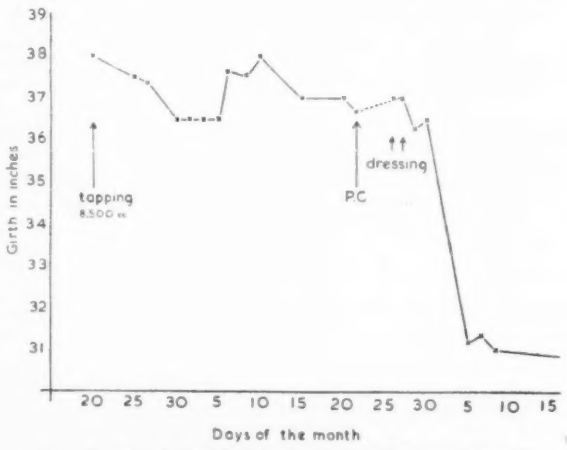

Fig. 1.—Graph showing the response to P.C. anastomosis of ascites as judged by girth measurement.

to have a very bad prognosis. They can be divided into two groups, those with ascites of insidious onset and those with ascites of acute onset. Ascites of insidious onset is resistant to treatment and often pre-terminal. It occurred in 52% of our severe, in 20% of our moderate and in none of our mild cirrhotics. 22 of our 47 ascitic patients are in this category.

Acute ascites frequently occurs at a time of temporary liver depression such as after hæmatemesis. Many of these patients die of the hæmorrhage in spite of emergency operation, or of the coma that often follows, or during subsequent build up for a shunt. This build up had often to be curtailed as soon as the serum albumin reached 3·2 grams/100 ml. for fear of further hæmorrhage. The reason why this form of ascites carries a better prognosis is seen when cirrhosis is divided into grades of severity. Only 39% of the severe cirrhotics had a hæmorrhage, while 76% of the moderate and almost all the mild cases had one or more. 25 patients in this series had acute ascites and were treated by "delayed emergency" shunts (to borrow Dr. Marc Iselin's phrase). The results were better in this group than in the patients without hæmorrhage. In assessing results, deaths from liver failure, even after a long interval, have been considered failures, but deaths from other causes not necessarily so.

Practical Management

Group 1. *Ascites alone.*—These patients are given an intensive course of medical treatment by or with the active help of the physicians. This treatment continues for at least three months. Many will lose their ascites but those whose albumin rises to 3·2 grams/100 ml. but are still ascitic may be offered operation. Porta-caval anastomosis is the treatment of choice, with a lieno-renal anastomosis as the alternative if the portal vein is shown to be thrombosed on venography, if there is excessive hypersplenism, or if the surgical approach is impossible. We have 5 cases of porta-caval anastomosis in this group with 2 successes, and 3 cases of lieno-renal anastomosis with 2 successes. 3 of the hepatic artery ligations had a serum albumin over 3·2 grams/100 ml., and 2 of these were successful (*see* Figs. 2 and 3).

Group 2. *Ascites with demonstrable varices.*—The treatment is the same as in Group 1. The risk of hæmorrhage if treatment is protracted should be weighed against the advantages of further medical treatment.

Group 3. *Ascites with hæmorrhage.*—(*a*) Ascites developing after a hæmorrhage, the ascites persisting in spite of medical treatment. A shunt is advised as soon as the patient is judged fit, often as little as two weeks after the hæmorrhage.

Fig. 2.

Fig. 3.—Illustrations showing abdomen before and after porta-caval anastomosis.

Jaundice is not a contra-indication. (*b*) Ascites developing after hæmorrhage which persists. A Sengstaken-Blakemore tube is passed and inflated for twenty-four hours, and is then cautiously deflated, left *in situ* for a further day, and removed. If the bleeding recurs, a Boerema-Crile operation is done through the left chest. If laparotomy is inadvertently done, a gastric approach to the varices is made, the pedicles being sutured through a gastrotomy. These operations are preferred as an emergency under-

taking to the more effective transection. Medical treatment is then carried out, and a shunt done two to three weeks later providing the albumin reaches 3·2 grams/100 ml.

The unfortunate group in whom the criteria for shunt operations are never fulfilled may be offered other operations for symptomatic relief. The Talma-Morison operation, ileo-entectropy and peritoneo-saphenous anastomosis are among these. The hepatic artery ligations come into this group and in all these the disappearance of ascites is a very gradual process by contrast to the shunt operations.

Mr. J. A. Girling for **Mr. Alan Hunt** (London):

A Case of Ileo-entectropy

Ileo-entectropy was devised by Dr. Charles Neumann of New York. It consists of the exposure of the mucous membrane of an isolated loop of terminal ileum in the peritoneal cavity with the aim of absorbing the ascitic fluid. Neumann has reported 10 cases with 5 deaths. Excluding cases with jaundice or œsophageal varices, there were 5 cases, 4 of them successful, and with no deaths.

We have performed the operation in one case. This was a married woman aged 32 with a history of two attacks of jaundice nine and eleven years previously. She was then in good health until ascites developed in the autumn of 1957. Paracentesis abdominis was necessary at shortening intervals. She was admitted to St. Bartholomew's Hospital in December 1957. Apart from her ascites she was in good health. She had no jaundice and barium swallow revealed no œsophageal varices. Serum albumin (3·0 grams/100 ml.) and pseudocholinesterase (26 units) were, however, low. Medical treatment resulted in some reduction in the rate of formation of ascitic fluid and a rise in serum albumin (3·3 grams/100 ml.).

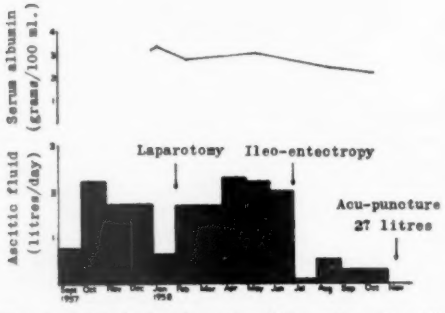

FIG. 1.—Graph showing rate of formation of ascitic fluid and level of serum albumin.

Laparotomy on 14.2.58 revealed a small cirrhotic liver. There were many vascular adhesions to the abdominal wall. Further adhesions around the porta hepatis made porta-caval anastomosis impracticable. She made a good recovery and returned home, although the ascites returned to its original level.

She was readmitted in June 1958, still in quite good health, although her serum albumin had llfaen to 2·8 grams/100 ml. and she had developed peripheral œdema.

Ileo-entectropy (2.7.58): the abdomen was reopened, and approximately 12 in. (30 cm.) of terminal ileum was isolated and split down the anti-mesenteric border. Fixation to the parietes in the right para-colic region as suggested by Neumann was not possible owing to vascular adhesions at this site. The cut edges were, therefore, turned back and sutured to one another and to their own mesentery. Recovery was stormy with an episode of hepatic pre-coma lasting three days.

Since operation her ascitic fluid has accumulated much more slowly. Her slow downhill course, has, however, continued, and she has increasing peripheral œdema. It is doubtful whether the operation will ultimately benefit this patient, although it has prevented the ascitic fluid from accumulating so rapidly.

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Professor B. W. Windeyer (London):

The Treatment of Ascites Due to Malignant Disease (*Summary*)

In discussing the management of ascites due to malignant disease, I shall limit myself to a consideration of certain types of reticulosis, carcinoma of the breast and carcinoma of the ovary. In the first group, the reticuloses, giant follicular lymphoblastoma, reticulum cell sarcoma, lymphosarcoma and Hodgkin's disease may be considered. Of these, giant follicular lymphoblastoma is most likely to give rise to ascites and in this condition, the development of serous effusions does not necessarily mean an immediate grave prognosis. Individual lesions are almost always radiosensitive. X-ray therapy to intra-abdominal deposits causing ascites will bring about rapid diminution in the masses and regression of ascites. Such treatment may be repeated in the event of recurrence and by this means the patient may be kept in reasonable health over

long periods of years. The disease tends, however, eventually to change to a lymphosarcoma or leukæmia. In reticulum cell sarcoma and lymphosarcoma, ascites may be a complication as a result of intra-abdominal deposits. Involvement of the mesentery of the gut wall may be a primary manifestation of the disease, but more frequently intra-abdominal involvement is a later manifestation when the disease has become generalized. Local irradiation by X-rays gives a variable response. In some cases the mass and the ascites have disappeared; in others, particularly if the disease is more generalized, it has not been possible to obtain more than temporary relief. Chemotherapy, by the use of nitrogen mustard, has sometimes given temporary regression with diminution of the amount of abdominal fluid. In Hodgkin's disease, with intra-abdominal disease, either as an early manifestation or occurring as a result of generalized disease, ascites has not been a marked feature. It does not give rise to symptoms comparable in gravity with other manifestations of the disease. The treatment of the ascites is part of the general treatment of Hodgkin's disease and does not present any particular features.

Ascites may occur in carcinoma of the breast due to intra-abdominal metastases. In a few cases where no metastases can be found in other parts of the body the local effects of the X-rays may produce worth-while palliation; and in others the instillation of radioactive gold into the peritoneum may produce similar benefit. In the majority, however, the development of ascites is part of the general picture of disseminated malignant disease, and the main direction of treatment has been to effect an alteration in the hormone state of the patient. To this end the first step has been the administration of œstrogens or androgens, according to the age of the patient, and in some cases has resulted in improvement, with reduction of the intra-abdominal fluid and even complete disappearance of the ascites. In those cases which have not responded to the administration of œstrogens or androgens, or have ceased to respond, hormonal surgery has been considered, either by adrenalectomy or hypophysectomy, or by cutting the stalk of the hypophysis. There are individual cases where ascites has been controlled by each of these procedures.

Carcinoma of the ovary provides by far the greatest number of cases of ascites that come to a radiotherapy department. The ascites may be due to large ovarian tumours or the multiple seedling deposits situated over the peritoneal surface. Even cases with quite a marked degree of ascites may still be operable, and prolonged freedom from disease may be obtained by surgical removal of the ovarian tumour. Laparotomy is indicated whenever the patient's general condition warrants it, if the pelvic neoplasm is not obviously irremovable. Post-operative irradiation should be given to the pelvis and lower abdomen after the removal of the ovarian carcinoma, and in inoperable cases radiotherapy should be given unless the general condition really precludes it. The majority of cases of ovarian carcinoma are not radiosensitive, but among the many disappointments there are some unexpected successes with the regression of an inoperable mass and sometimes disappearance of ascites. The more general use of supervoltage apparatus has made it possible to give more efficient radiation to the abdomen, with less distress, less sickness and greater chances of complete regression. Instillation of radioactive gold may produce excellent palliation, not only in those cases with multiple seedling peritoneal deposits but also sometimes in patients with solid palpable tumours.

Ascites due to malignant disease can give rise to great distress and is extremely difficult to control. There are, however, some methods of treatment which are worth while and which can sometimes, if applied with judgment and proper restraint, be of inestimable value to patients in relieving distress in the last months of life.

Dr. N. R. Mackay (Guildford):

Effusions of Malignant Origin (*Summary*)

At the Royal Marsden Hospital—during the period 1950 to 1956—235 cases of peritoneal or pleural effusions were treated by radioactive colloidal gold (Mackay, 1957). The technique adopted for intracavitary instillation is simple. The peritoneum is punctured in the para-umbilical region by a trocar and cannula of at least 15 cm. length with two additional lateral openings near its distal end, and the peritoneal cavity emptied of fluid as far as possible. A dose of between 120 to 130 millicuries (mc.) is then administered. Provided that the patient is not in a poor general condition this dose does not give rise to any appreciable systemic upset. On return to the isotope ward the patient is nursed in a special tipping bed with frequent changes in posture in order to insure an even distribution of the colloid. About four hours after injection the abdomen is scanned with a counter to determine the distribution.

Table I shows the result of intracavitary radioactive colloidal gold treatment. "Fluid inhibited" means that following the instillation of gold further formation of fluid was completely arrested or markedly reduced. "Probably inhibited" means that there were longer intervals between aspirations following colloidal gold treatment. A considerable proportion of cases

TABLE I.—235 EFFUSIONS—RESPONSE TO INTRA-CAVITARY ^{198}Au

Primary	Site	Fluid inhibited	Probably inhibited	No effect	Not known	Rejected
Breast	61 Pleura	15	10	9	26	1
	15 Peritoneum	5	1	1	8	—
Ovary	3 Pleura	1	—	1	1	—
	68 Peritoneum	8	—	5	31	24 (Prophylactic)
Lung	19 Pleura	4	4	4	5	2
Unverified ..	2 Pleura	1	—	—	1	—
	16 Peritoneum	6	—	1	9	—
Reticuloses ..	12 Pleura	7	1	3	1	—
	3 Peritoneum	3	—	—	—	—
Colon	11 Peritoneum	2	—	1	4	4 (Prophylactic)
Miscellaneous ..	3 Pleura	—	—	1	—	2
	5 Peritoneum	4	—	—	1	—
Stomach ..	7 Peritoneum	—	—	—	7	—
Uterus: body ..	2 Pleura	1	—	1	—	—
	6 Peritoneum	1	—	2	2	1
Uterus: cervix ..	1 Pleura	—	—	1	—	—
	1 Peritoneum	1	—	—	—	—

had to be allocated to the "Not known" category. These included patients dying within four weeks of treatment, patients who had had only one aspiration before treatment and in whom therefore it was impossible to determine the rate of fluid accumulation. The rejected group includes prophylactic intraperitoneal irradiation, most commonly following rupture of a malignant ovarian cyst at operation. Also included are patients who had usually been told at some outside hospital that their only hope depended on the injection of gold and in whom only a few token millicuries were injected for psychological reasons.

The cause of ascites in malignant disease is not known. The following factors could be responsible:

(1) Venous and lymphatic obstruction by tumour causing an increase in pressure within the vessels and a consequent rise in transudation and interference with absorption.

(2) Exudation of fluid from raw neoplastic surfaces. This is unlikely to play a significant part. At autopsy one frequently observes cases of lung, breast, or ovarian cancer where there are masses of neoplastic tissue in the peritoneum or pleura but no appreciable fluid; and conversely other cases with no appreciable evidence of serous involvement but large quantities of fluid which had required frequent tapping.

Why radioactive colloidal gold on occasions arrests the formation of peritoneal fluid is also not known. It is unlikely that it is due to the superficial irradiation of neoplastic masses. The colloidal particles are rapidly removed from the peritoneal cavity and deposited in the sub-endothelial layer of the peritoneum. It is possible that fibrosis in this situation involves the sub-endothelial blood and lymph capillaries and in some way results in the inhibition of fluid accumulation. In addition radioactive colloidal gold can give rise to areas of fibrinous reaction with the formation of adhesions between the visceral and parietal layers, resulting in a reduction in the size of the cavity and the surface area of serous membrane capable of secreting fluid.

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Mr. M. Reilly (Plymouth):

The problem of malignant ascites is a widespread and distressing one. If one works at a distance from university and research centres one cannot refer every case for radioactive gold. Assuming that this treatment works mainly by obliterating potential space for the accumulation of fluid rather than by its lethal action on malignant cells, I thought that a sclerosant such as talc might act as an efficient substitute. During the last three or four years I have therefore used talc powder, which is either tipped in and stirred round at laparotomy or instilled in suspension through a cannula. The amount of talc used is roughly 1 oz. (30 grams). I have treated seven or eight cases in this way with reduction of ascites formation, the most dramatic case having the amount of ascitic fluid obtained by paracentesis reduced from a gallon a week pre-operatively to two or three pints a month post-operatively. I have had no case of intestinal obstruction from adhesions.

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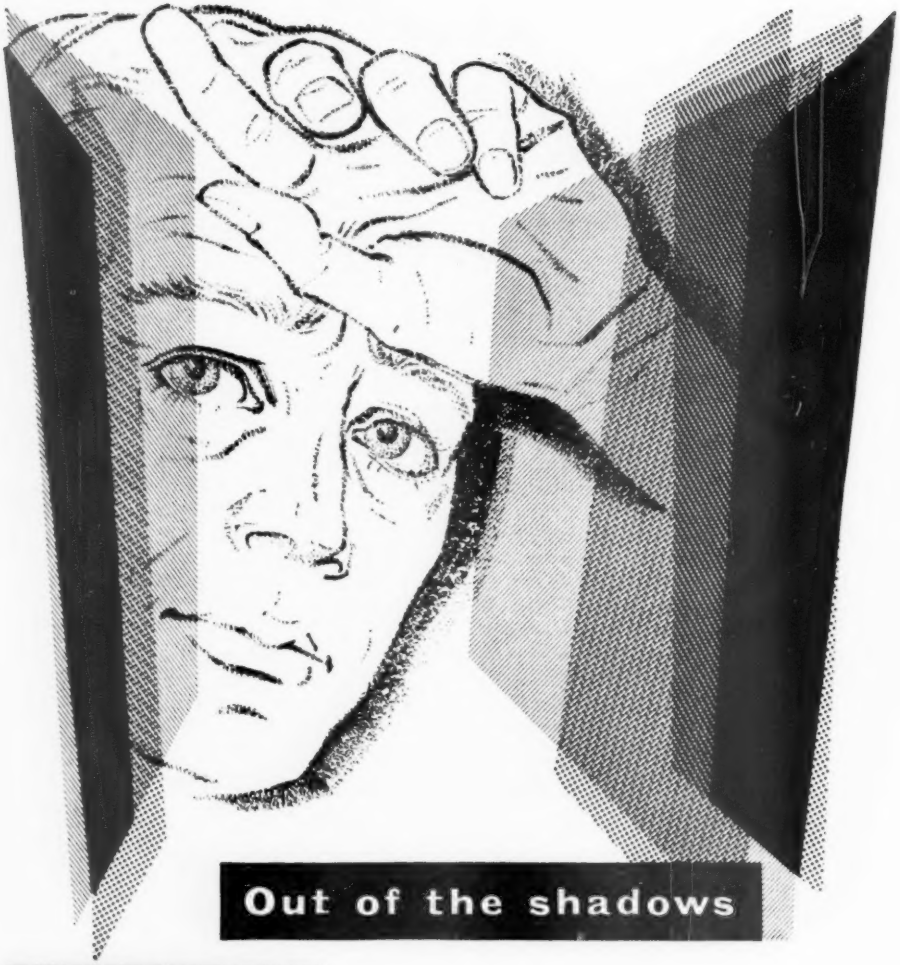

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SAFE AND EFFECTIVE IN

PSYCHOSES Particularly Schizophrenia [1 & 2]

NEUROSES Tension states and patients with obsessional traits

GENERAL MEDICINE Agitated states in the elderly [3]

1. Am.J.Psychiat. 1958, **114**, 1034.
2. A.M.A. Arch. Neurol.Psych. 1958, **80**, 481.
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SEARLE HIGH WYCOMBE, BUCKS.

DA : P39

Section of Endocrinology

President—Professor F. T. G. PRUNTY, M.D., F.R.C.P.

Meeting
November 26, 1958
(continued from *Proceedings*, March 1959, p. 182)

Hyperparathyroidism.—MICHAEL HARRISON, M.B., M.R.C.P., and RUSSELL FRASER, M.D., F.R.C.P.

Mrs. H. C., aged 58.

History.—Four years ago: Weakness of legs, at times so severe that they gave way under her. Swelling of knees without much pain. X-rays at that time showed erosions of femoral surface of patellae (Fig. 1), and she was thought to have rheumatoid arthritis. Subsequently anorexia and weight loss (3 st.) developed, together with thirst and polyuria. For past eighteen months only she also complained of backache and getting shorter, and since then had lost 2½ in. in height.

FIG. 1.

Past illnesses.—1940: Duodenal ulcer.

On examination (Hammersmith Hospital, October 1958).—Generalized weakness and hypotonia, but brisk reflexes. Dorsal kyphosis. Blood pressure 120/75. Pea-sized nodule left lower pole of thyroid. Knees: Swollen joints and metastatic calcification.

Investigations.—Blood: Calcium 15·6, phosphorus 1·9 mg./100 ml. Alkaline phosphatase 135 K.-A. units. Urea 55 mg./100 ml. Potassium 3·1 mEq./l. Differential agglutination test negative.

Urine: Maximum specific gravity 1010—no change after Pitressin. Phosphorus excretion index +0·73 (normal ±0·12 — Nordin and Fraser, 1956). Calcium 186 mg./twenty-four hours, on low calcium intake.

X-rays: Thin bones with subperiosteal erosions. Barium swallow: indentation of œsophagus on left side at level of sternal notch.

Bone turnover of calcium by strontium tracer test (Fraser, 1957) = 5·7 grams calcium/day (normal 0·5 grams/day).

Operation (Professor Ian Aird).—Large parathyroid adenoma removed from left lower pole of thyroid.

Comment.—This patient illustrates the difficulty which may be encountered in diagnosing hyperparathyroidism at an early stage. Unusual features were the rheumatoid-like erosions, the absence of renal calculi despite severe bone disease, and a normal urine calcium excretion. At Hammersmith Hospital we have seen 3 patients with similar erosions of the patella, all of whom proved to have hyperparathyroidism. The value of the strontium tracer test in diagnosis is illustrated.

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Post-partum Hypopituitarism.—D. N. PHEAR, M.D., M.R.C.P. (for H. JOULES, M.D., F.R.C.P.).

Mrs. M. S., aged 48.

History.—Aged 18 and 20: Normal pregnancies. Aged 30: Stillbirth with very severe post-partum hæmorrhage following which she became unconscious. She recovered with blood transfusions, but she did not lactate and her periods did not return. She felt cold and tired, and lost pubic and axillary hair. Aged 32: Menstruated once, with subsequent normal pregnancy, and delivery by Cæsarean section. Again there was no lactation and no further menstruation.

On examination.—Pale, dry skin with absent axillary and scanty pubic hair. Atrophic genitalia. Some pigmentation of parts exposed to sun.

Investigations.—Radioiodine studies (Dr. A. W. G. Goolden): Reduced extrarenal disposal rate. T=2·4 (normal 2·8—13). Water clearance test: Delayed water excretion. 17-ketosteroid excretion: 3·2 mg./twenty-four hours. Chest X-ray: Bilateral apical fibrosis.

Progress.—Much improvement with cortisone and thyroid.

Comment.—This patient presents a classical picture of post-partum pituitary necrosis. Subsequent pregnancies in such patients are rare, but usually result in recovery by producing hypertrophy of the remaining pituitary tissue (Sheehan, 1939).

Pulmonary tuberculosis, active or quiescent, is very common in these patients (Simpson, 1883). It is interesting that diagnosis in such a patient can be delayed for eighteen years. Much chronic ill-health must result from post-partum hypopituitarism, though this complication is now less frequent with modern methods of transfusion and the use of ergometrine during delivery.

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Cushing's Syndrome with Pituitary Tumour and Pigmentation.—J. R. REES, M.R.C.P. (for R. I. S. BAYLISS, F.R.C.P.).

Mr. J. L., aged 28.

First admission (November 1953).—Six months' history of increasing obesity, fullness of face and mild depression. Three weeks' history of striae on thighs and upper arms and diminished potency. Typical appearances of Cushing's syndrome. Blood pressure 160/110.

Investigations.—Blood count, serum electrolytes, glucose tolerance, X-ray of skull, chest, spine and presacral air insufflation all normal. Urinary 17-ketosteroid excretion 35 mg./day (mean of 7 estimations). Plasma 17-hydroxycorticosteroids 24 μg./100 ml. After ACTH stimulation (20 units i.v. over eight hours) urinary 17-ketosteroid excretion 74 mg./day and plasma 17-hydroxycorticosteroid level 75 μg./100 ml.

Operation 16.11.53 (Mr. Selwyn Taylor).—Bilateral adrenal hyperplasia. Whole of right adrenal removed (11·5 grams) and three-quarters of left (5·5 grams). Good response to operation with loss of cushingoid features and fall in blood pressure to 145/90. Urinary 17-ketosteroid excretion 7 mg./day and plasma 17-hydroxycorticosteroids 9 μg./100 ml. following operation, with insignificant response to ACTH stimulation. Pigmentation first noted in mouth in January 1954.

Second admission (January 1956).—Recurrence of depression with intermittent bitemporal headache and increasing pigmentation. Found to have recurrence of Cushing's syndrome with mild pigmentation. Blood pressure 180/120.

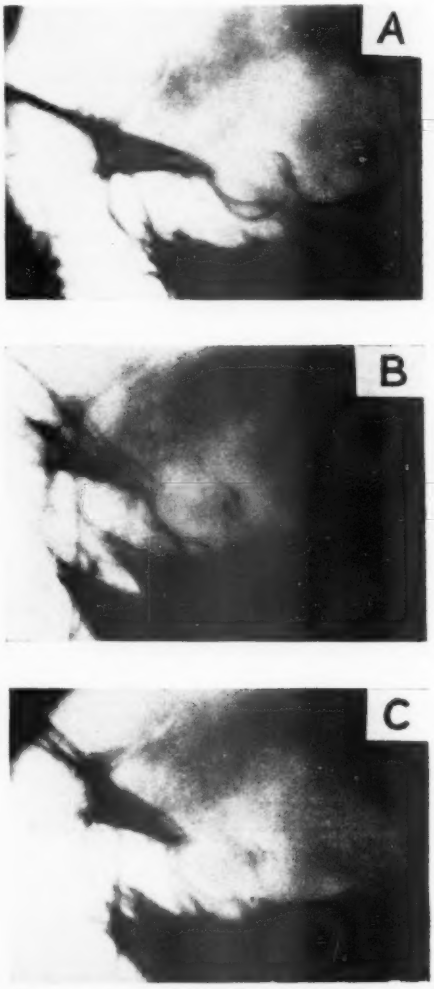

FIG. 1.—Comparative coned views of pituitary fossa. A. (November 1953), normal. B. (June 1957), shows no increase in diameter (14 mm.) but definite decalcification of the dorsum sellæ. C. (June 1958), shows expansion of the pituitary fossa (diameter 22 mm.) and definite evidence of pituitary tumour.

Investigations.—Blood count, serum electrolytes and glucose tolerance normal. Urinary 17-ketosteroid excretion 25 mg./day, urinary 17-hydroxysteroid excretion 50·1 mg./day. After fluorohydrocortisone 8 mg. daily for five days no change occurred in urinary 17-hydroxysteroid excretion but 17-ketosteroid excretion fell to 11·4 mg./day.

Operation 8.3.56 (Sir Stanford Cade).—Left adrenalectomy. The adrenal remnant was found to be hypertrophied (weight 13 grams) and histology showed diffuse hyperplasia. Good response to operation and discharged on oral cortisone 25 mg. b.d. increasing to 25 mg. t.d.s. In August 1956 his depression became severe and he was admitted to a mental hospital following a suicidal attempt.

Third admission (June 1957).—Transferred from mental hospital with complaint of weakness, impotence and mild frontal headache. Receiving supplement of cortisone 75 mg. daily and fluorohydrocortisone 0·5 mg. alternate days. Examination showed no evidence of Cushing's syndrome but deep generalized pigmentation with heavy buccal involvement was seen.

Investigations.—Urinary 17-ketosteroid excretion 7·5 mg./day. Plasma ACTH (Dr. Barbara Clayton) 38 mU./100 ml. Plasma melanophore-expanding hormone 1 i.u./7 ml. plasma. Skull X-ray considered normal, but definite decalcification of dorsum sellæ is seen although the transverse diameter of the pituitary fossa is not increased.

Fourth admission (June 1958).—History of increasing pigmentation and intermittent frontal headache for one year, with diplopia and blurring of vision for two weeks.

On examination.—Blood pressure 130/80. Not cushingoid. Deep cutaneous and buccal pigmentation. Incomplete bitemporal hemianopia. Partial left III and VI nerve paralysis.

Investigations.—Urinary 17-kestoteroid excretion 9 mg./day. Urinary 17-hydroxysteroid excretion 25·8 mg./day (mean of 4 estimations). Urinary F.S.H. excretion less than 6 mouse units/twenty-four hours. Plasma ACTH level less than 7·5 mU./100 ml. B.M.R. −13%. Skull X-ray: enlarged pituitary fossa. Air encephalogram: elevation of anterior end of third ventricle with obliteration of optic and infundibular recesses.

Operation 8.8.58 (Mr. G. Macnab).—Removal of pituitary tumour.

Histology (Dr. A. G. Pearse).—A mucoid cell adenoma (basophil adenoma) without evidence of malignancy. The tumour cells showed excellent preservation of mitochondria and considerable activity of the DPN-linked dehydrogenases. Succinic dehydrogenase activity rather low. Uneventful recovery from operation. Maintained on cortisone 75 mg. daily and thyroxine 0·2 mg. daily. There was little change in the pigmentation until November 1958, three months after removal of the pituitary tumour, when definite depigmentation became apparent.

Comment.—This patient was first reported in 1954 (Bayliss and Hunter, 1954) and shows the liability of young patients with Cushing's syndrome to relapse despite apparently adequate subtotal adrenalectomy. The striking features of this case are the development of pigmentation and the discovery of a pituitary tumour. Pigmentation was not present before partial adrenalectomy and was only slight before the second operation. It became severe after total adrenalectomy when a marked elevation of the plasma melanophore-expanding hormone was demonstrated. This resembles the case of Nelson *et al.* (1958) in whom a chromophobe pituitary tumour was found, and differs from other cases (Edmunds *et al.*, 1958) in whom pigmentation developed with the Cushing's syndrome and subsided after adrenalectomy. The extension of a basophil adenoma outside the pituitary fossa to produce pressure symptoms must be extremely unusual and suggests it had been present longer than most or that its growth had been more rapid. Nelson *et al.* (1958) suggested in their case that the pituitary tumour might have been a sequel of adrenalectomy. We have insufficient evidence to decide this point in our patient. The depigmentation following removal of the tumour suggests that the excess of melanophore-expanding hormone was produced by the basophil adenoma itself. Since pigmentation only became severe after total adrenalectomy it is probable that this operation was a powerful stimulus to pituitary activity, facilitating increased growth of the basophil adenoma, or even its development.

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Meeting
January 28, 1959

The Effects of Sodium Depletion on Bone Sodium Metabolism

By Donald S. Munro, M.D., M.R.C.P.

Sheffield

It has been known for some years that bone mineral undergoes constant turnover throughout life (Shohl, 1939) and that bone is the only tissue in which the sodium concentration is higher than in extracellular fluid (Harrison *et al.*, 1936). However, it was not until the use of radioisotopes gave more accurate information about the dynamics of bone mineral metabolism that the potential importance of bone in sodium metabolism was appreciated (Hevesy, 1955; Neuman and Neuman, 1958).

Analysis of the whole human body, though limited to a few observations, has shown that the total sodium content is approximately 5,000 mEq. (Widdowson *et al.*, 1951; Forbes and Lewis, 1956). Of this total, probably not less than one-half is in bone. Ever since the earliest studies with radioactive sodium isotopes it has been realized that bone sodium does not exchange completely within periods adequate for complete exchange in all other tissues (Kaltreider *et al.*, 1941). Later work has repeatedly confirmed this observation in different species. For example, Bauer (1954) found in rats that only 30–40% of bone sodium exchanged with injected radiosodium within twenty-four hours and similar values have been reported in rabbits (Davies *et al.*, 1952), in dogs (Edelman *et al.*, 1954) and in man (Edelman *et al.*, 1952; Miller and Wilson, 1953; Miller *et al.*, 1954).

It is clear therefore that alterations in bone sodium metabolism may affect both sodium balance studies and the measurement of exchangeable sodium in man. It is known that loss of sodium from the body lowers bone sodium content (Bergstrom, 1955; Nichols and Nichols, 1956; Levitt *et al.*, 1956) and bone sodium content may rise after sodium loading (Nichols and Nichols, 1957) and after parathyroidectomy (Nichols and Nichols, 1958).

Until recently little was known about the effect of alterations of bone sodium content on bone sodium exchange. There are great difficulties in attempting to study alterations in bone sodium exchange in man during life. Using an external counting technique Miller *et al.* (1954) were able to obtain information about the penetration of radiosodium into bone in human subjects on a diet of low sodium content and in a steady state of sodium balance. Their method was not sufficiently sensitive to attempt to follow alterations under conditions of altering sodium balance. For this reason the effects of acute sodium depletion were studied in rats. In the first instance, it was established that the bone content of sodium increased with age, whilst the proportion available for exchange declined (Munro *et al.*, 1957). Thereafter the effects of acute sodium depletion were studied in groups of rats selected by weight. Sodium was removed from the body by peritoneal dialysis lasting four hours (Bergstrom and Wallace, 1954). On the morning of the next day the rats received an intraperitoneal injection of radiosodium and were killed twenty-four hours later. The whole procedure thus lasted forty-eight hours and the rats were fed on a diet of rice and distilled water throughout the experiment. Samples of blood and bone were obtained for measurement of radioactivity and sodium content.

It was confirmed that the procedure reduced the bone content of sodium. In rats of between 50 and 100 grams, for example, the bone sodium content of the depleted rats was 210 mEq./kg. dry bone, compared with 247 mEq./kg. dry bone in controls. In older animals the decrease in bone sodium was not so pronounced. Surprisingly, in both groups the amount of sodium available for exchange with the injected radiosodium was not altered. It is evident that the transfer of sodium from bone to extracellular fluid must in the first instance be from the exchangeable fraction which, by definition, is able to participate in ionic exchange with the extracellular fluid. These results suggest therefore that, after depletion, some sodium in bone which was not originally available for exchange had become exchangeable so that the absolute amount available remained constant. In the younger animals, the serum sodium level did

not fall after sodium depletion but in older animals which released sodium from bone less readily the serum sodium fell from 149 to 139 mEq./l.

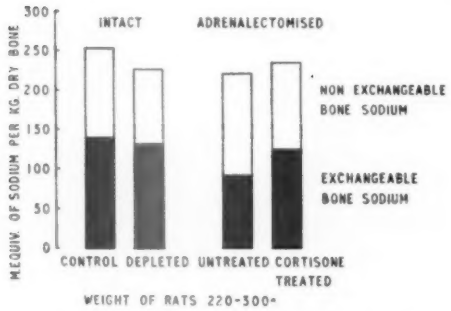

FIG. 1.—The effect of sodium depletion on bone sodium metabolism in intact and adrenalectomized rats.

Because of the known importance of the adrenal glands in sodium metabolism, attention was next directed towards the effect of adrenalectomy on bone sodium. In contrast to the normal renal sodium conservation of intact animals, adrenalectomized rats (220–300 grams) fed on a diet of low sodium content continued to excrete sodium in their urine. Within forty-eight hours the bone sodium content rapidly declined from 256 to 222 mEq./kg. dry bone and there was a slightly less abrupt fall in serum sodium level from 149 to 132 mEq./l.

The injection of radiosodium revealed that the drop in bone sodium content was associated, in these circumstances, with a reduction in the exchangeable fraction. At the time of death sodium intake had been restricted for seventy-two hours and the animals felt cold and limp. When treated with cortisone acetate during the period of sodium restriction, however, their general condition was improved and though bone sodium did fall, the effect on exchange was much less striking, so that the alterations corresponded more closely to the effects of sodium depletion in intact animals (Fig. 1). The changes could be completely avoided by the simultaneous administration of cortisone and saline. A possible explanation for the decreased exchange in untreated, adrenalectomized rats is that the circulation was so impaired that the sodium isotope was not carried fully into the bone (Munro *et al.*, 1958).

The results of animal experiments cannot be assumed to be directly applicable to man. Nevertheless, there is a close resemblance between the structure of bone mineral in different species (Neuman and Neuman, 1958), and the bone sodium content and exchange in health are also similar. It is therefore highly probable that sodium depletion in man is associated with changes in bone sodium metabolism resembling those encountered in these experiments. Moreover, such changes provide a possible explanation for the discrepancies in balance studies which have been noted in earlier reports (Wilson and Miller, 1953; Atchley *et al.*, 1933; Flanagan *et al.*, 1950).

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An Inhibitor of Adrenal Steroid 11-hydroxylation

By J. S. Jenkins, M.D., M.R.C.P.

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Inhibition of adrenal cortical function by compounds having a direct action on steroid biosynthesis has been most extensively studied in the case of the drug amphenone, synthesized by Allen and Corwin in 1950. Several workers have demonstrated that adrenal steroid secretion could be reduced by this substance both in the dog and in man, but unfortunately the toxic effects of amphenone have precluded its widespread use, and have led to the search for further inhibitory agents.

Recently the compound 2-methyl-1-2-bis(3 pyridyl)-1-propanone, known as D.P.P. or S.U.4885, as it will be referred to in this paper, has been synthesized by Allen and Bencze (Chart *et al.*, 1958), and the action of this drug on adrenal cortical secretion has been studied both in the dog and in man.

Experiments were carried out on normal dogs anæsthetized by sodium pentobarbitone. An intravenous infusion of ACTH was given to obviate any changes in adrenal stimulation. The right lumbo-adrenal vein was cannulated and adrenal venous blood was collected at timed intervals. The plasma was separated and total 17-hydroxycorticoids were estimated by the Nelson and Samuels (1952) method. Individual steroids were characterized by paper chromatography, identification being carried out by a comparison of running rates of the free and acetylated substance with known standards in different chromatographic systems, ultraviolet light absorption, blue tetrazolium, and phenylhydrazine reactions, sulphuric acid absorption spectra and in some instances infra-red spectroscopy. Quantitative estimation was carried out by elution of the steroids off the paper and application of the phenylhydrazine or blue tetrazolium reactions.

A single intravenous injection of 75 mg. of S.U.4885 per kg. caused a fall in total 17-hydroxycorticoids in the adrenal venous blood of the dog to approximately 10% of the initial values within ten minutes, rising to about 75% in three hours.

A smaller dose of 5 mg./kg., given intravenously over thirty minutes, produced no decrease in total 17-hydroxycorticoids. When the infusion was increased to 75 mg./kg. a reduction in steroid output was again observed.

The most striking effect of the drug, however, was seen when the individual plasma steroids were characterized.

After a single injection of 75 mg. of S.U.4885 per kg. hydrocortisone fell from 7·0 μg. per minute to immeasurable levels within ten minutes but even after seven hours the value was still only 0·9 μg., returning to approximately initial levels by twenty hours. Concomitant with the prolonged inhibition of hydrocortisone was the appearance of 11-desoxyhydrocortisone, Reichstein's substance S, which rose from previously undetectable levels to 5·6 μg. five hours after the injection of the drug. Corticosterone, initially present in large amounts in the control sample, disappeared and was replaced by desoxycorticosterone.

When only 5 mg. of S.U.4885 per kg. was administered, hydrocortisone was again inhibited contrary to what would be expected from the total 17-hydroxycorticoid values, the major part of which was evidently due to substance S. Desoxycorticosterone also appeared once more in place of corticosterone. The infusion of 75 mg./kg. caused a temporary reduction in total steroid output but again the predominant component was substance S.

In view of these results it was of interest to compare the effect of amphenone on the steroid pattern when given in a dosage equivalent to 75 mg./kg. of S.U.4885. This caused a temporary reduction in hydrocortisone and corticosterone. During the following three hours the levels of both steroids gradually rose but without any evidence of 11-desoxy compounds.

Following these experiments carried out in the dog, it was important to study the action of S.U.4885 in man, bearing in mind that adrenal inhibitory agents sometimes show considerable species specificity. 8 patients were studied including 4 cases of Cushing's syndrome, and 4 who showed no evidence of adrenal abnormality. 5 of the patients received the drug intravenously.

2 grams of the drug was administered as an intravenous infusion over eight hours to a patient suffering from Cushing's syndrome. Tetrahydrocortisone (THE) and tetrahydrohydrocortisone (THF) were temporarily reduced but this was accompanied by the appearance of large quantities of tetrahydro-S (THS) previously

reported by other workers to be a major urinary metabolite of substance S.

Plasma free and conjugated corticosteroids were also studied in the same patient. In this case an eight-hour infusion of ACTH was given and a blood sample taken at the end of four hours. 2 grams of S.U.4885 was then administered intravenously over a further four hours and at the end of this period there was a reduction in both hydrocortisone and tetrahydrohydrocortisone with the appearance of substance S and very large quantities of tetrahydro-S.

3 patients were given S.U.4885 orally in amounts ranging from 3–12 grams daily, divided into four-hourly doses. In every case total urinary 17-hydroxycorticoids increased considerably following administration of the drug and remained elevated above the control values up to two days after it was discontinued. Urinary 17-ketosteroids were also elevated. The 17-hydroxycorticoids include THE, THF and THS. In a patient receiving 3–6 grams of the drug there was a great increase in the excretion of THS but THE and THF remained essentially unchanged. It appears that this dosage orally only partially inhibits 11-hydroxylation and it would seem that any tendency for hydrocortisone to fall would be followed by increased output of ACTH, thereby restoring to normal the levels of hydrocortisone and its urinary metabolites, but stimulating still further the production of substance S, and also elevating 17-ketosteroid excretion.

When, however, 6–12 grams of the drug was given to a patient, this was sufficient to inhibit 11-hydroxylation more intensively and a marked fall in THE and THF was observed, the output of THS rising to 28·5 mg. per twenty-four hours. The elevated levels of 17-hydroxycorticoids seen in all cases was therefore due to the large amounts of THS excreted. The urine of 2 patients was also examined for evidence of tetrahydrodesoxycorticosterone (THDOC), a urinary metabolite of desoxycorticosterone. In both cases a substance was identified which behaved chromatographically and spectrophotometrically in a similar manner to that reported for authentic tetrahydrodesoxycorticosterone. Quantitative determination yielded values which rose from initially undetectable levels to a maximum of 0·9 mg. per twenty-four hours in one case, and 0·7 mg. in the other, whilst receiving the drug.

Toxic effects were much less prominent with S.U.4885 than with amphenone. No untoward effects were seen in any of the patients receiving the drug intravenously. Nausea and gastric discomfort, however, were experienced by all patients taking 6 grams or more orally. This was partly controlled by giving aluminium hydroxide. Dizziness was complained of by a patient taking 12 grams daily, but drowsiness, which is such a prominent feature with amphenone therapy, was not seen in any patient.

In conclusion, S.U.4885, when given in large doses to the dog, caused a fall in total adrenal corticosteroid secretion, but this was of relatively short duration and was followed by a prolonged period during which 11β-hydroxylation alone was inhibited and substance S and desoxycorticosterone were secreted. In the relatively smaller doses administered to the patients no fall in total steroids was seen, but the large quantities of 11-desoxy compounds present in blood and urine again indicated that the inhibitory action of this drug is directed particularly at the 11β-hydroxylase enzyme system. In this respect the action of S.U.4885 differs considerably from that of amphenone, which causes a generalized inhibition of steroid synthesis with no selective effect on 11β-hydroxylation. The effect of S.U.4885 is in fact comparable with the congenital failure of 11β-hydroxylation described by Eberlein and Bongiovanni (1956) in some cases of adrenal hyperplasia. These patients also excrete large quantities of THS and also THDOC, which may perhaps be a factor in the hypertension seen in this type of congenital adrenal hyperplasia. None of the patients receiving S.U.4885 showed any change in blood pressure, but this may have been due to the relatively short period of administration since THDOC was tentatively identified in the urine of 2 cases.

From these considerations it would not appear that S.U.4885 has an immediate clinical application. Nevertheless, selective inhibition of an adrenal enzyme system is of considerable interest, although the exact mode of action remains to be elucidated. It seems probable that further compounds will be elaborated, the study of which may lead to increased knowledge of the mechanisms of adrenal steroid biosynthesis.

(A more detailed paper relating to this subject will appear in the *British Medical Journal*.)

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The Effect of Hormones on Phosphate Transport Across the Renal Tubule [*Summary*]

By J. ANDERSON, M.D., M.R.C.P.

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ONE of the important actions of hormones is the regulation of the transfer of ions, particularly phosphate, across the cell walls of various organs. The kidney is an interesting organ to study in that it is possible to investigate experimentally the transfer of phosphate across the renal tubule in man. The maximum tubular reabsorption of phosphate (Tm_p) is a measure of the amount of phosphate transferred in unit time across the cells of the renal tubule.

It is well known that parathyroid hormone influences the tubular reabsorption of phosphate and patients with hyperparathyroidism have a low Tm_p (Anderson, 1955*a*). It is not often realized that this is only one of several hormones that act on this mechanism. The following studies were undertaken to test the validity of this hypothesis.

The Tm_p has been determined in the following studies by means of a three-hour phosphate infusion (Anderson, 1955*b*).

3 patients, who had rheumatoid arthritis for many years and were about to receive cortisone, had control infusions before treatment and a further infusion while on 75 mg. of cortisone a day; in each case, the cortisone depressed the Tm_p. 3 normal subjects had phosphate infusions before and while taking 100–200 mg. of cortisone a day; in 2 subjects the Tm_p fell with cortisone, in the other subject there was no change in spite of the fact that he showed signs of an excess of circulating corticoid. 2 patients with Addison's disease had a phosphate infusion while receiving 37·5 mg. of cortisone a day and the Tm_p in each of these patients was within the normal range. Thus, an excess of cortisone in man depresses the Tm_p below normal. Roberts and Pitts (1953) obtained similar results in dogs.

In thyrotoxicosis the Tm_p tends to be raised in patients who are mildly thyrotoxic. However, those with more severe thyrotoxicosis have a depression of the Tm_p below normal. Beisel *et al.* (1958) have shown that 1 mg. of triiodothyronine depresses the Tm_p in dogs after four hours.

2 patients who had myxœdema had a high Tm_p and this fell towards normal on treatment with dried thyroid.

2 patients with active acromegaly had a high Tm_p. They also showed the typical stigmata and had glycosuria and a diabetic type of glucose tolerance curve.

One patient with hypogonadism had a high Tm_p before treatment but 250 mg. of microcrystalline testosterone a month for three months had no effect on his Tm_p. However, his fasting plasma inorganic phosphorus concentration fell from 4·5 to 3·8 mg. per 100 ml.

Thus cortisone, thyroid hormone, growth hormone and possibly testosterone play a part in the regulation of the transfer of inorganic phosphate across the renal tubule.

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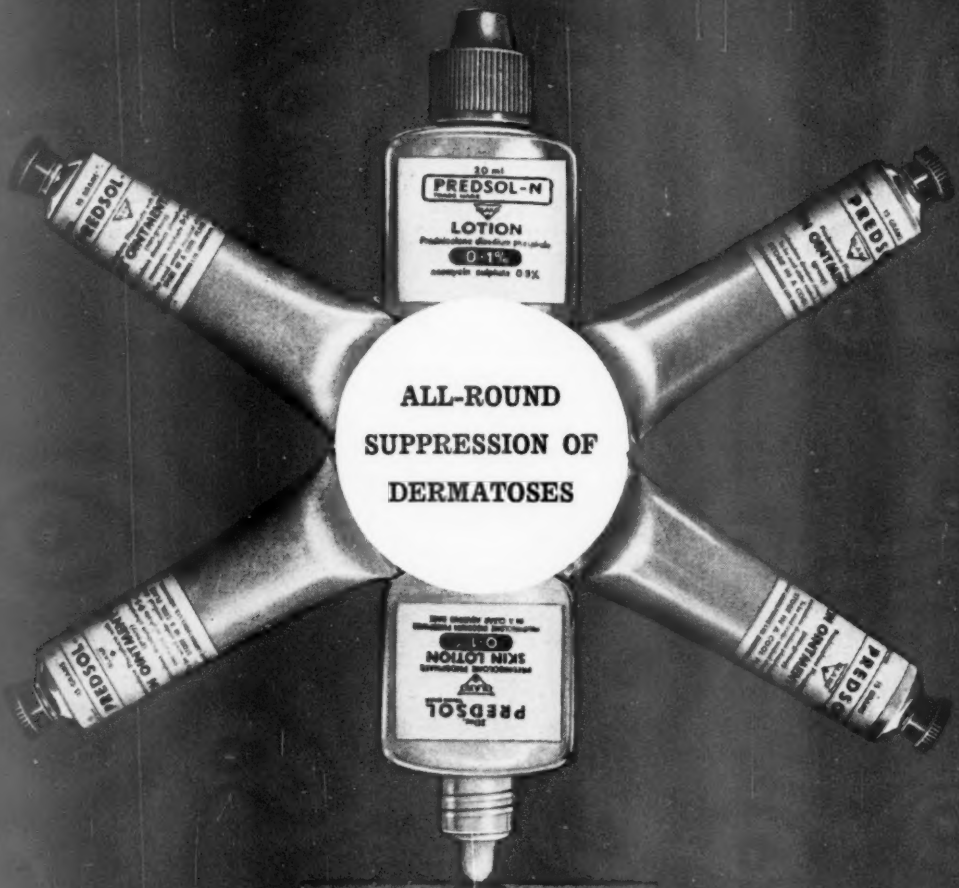

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Meeting
October 27, 1958

Dr. W. G. SENIOR delivered his Presidential Address entitled **The Child and Us.**

The Address has been reported in the *British Dental Journal*, **106**, 111, February 3, 1959.

Meeting
January 26, 1959

Further Studies on the Growth of the Human Face

By JAMES H. SCOTT, M.D., D.Sc.
Belfast

IN a previous paper (Scott, 1954) certain features of facial growth in man were discussed. Here it is proposed to consider some of the same matters in greater detail, and also some new material, so as to give a more complete picture of our present knowledge of this complex problem.

Growth at Sutures

Pritchard *et al.* (1956) have given a fuller and more accurate account of the structure of growing sutures. Fig. 1, from their paper, shows the layers of soft tissue between the bony elements of a typical facial suture during the period of active growth of new bone at the adjacent edges of the bones bounding the suture. Selman and Sarnat (1955) have demonstrated by the use of metallic implants that at a suture one bone may grow faster than another, emphasizing the fact that at each suture there are two "growth centres", one for each bony element.

Fig. 2 (A–C) illustrates the changes in suture structure at the mid-palatal suture in man from about three and a half months of fœtal life to the

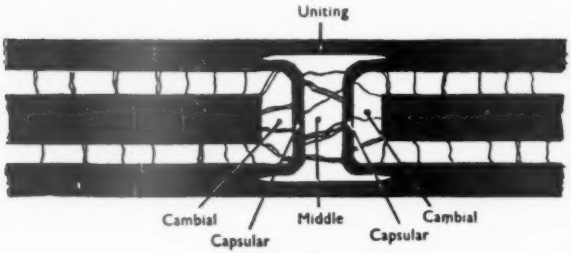


FIG. 1.

←FIG. 1.—Diagram showing the structure of a growing suture (by courtesy of Pritchard *et al.* and the *Journal of Anatomy*).

FIG. 2 (*below*).—Changes in suture structure with age.

A, mid-palatal suture 70 mm. C.R. human fœtus. × 50.

B, mid-palatal suture 135 mm. C.R. human fœtus. × 60.

C, mid-palatal suture child 1 year old. × 60.

D, zygomatico-temporal suture 250 mm. C.R. human fœtus. × 40.

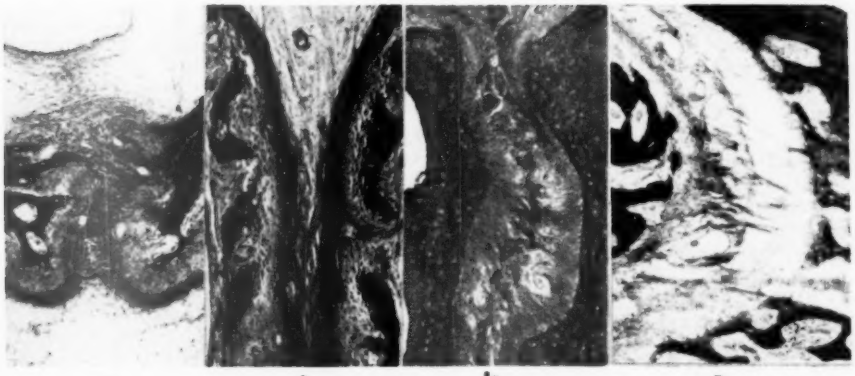


FIG. 2.

first year after birth. These changes can be tabulated as follows:

(1) A gradual reduction in the osteogenetic zone as the rate of bone deposition at the suture slows down.
(2) A greater density and "knitting together" of the collagenous fibres in the capsular and middle zones.
(3) The development of collagenous fibre bundles which directly unite the adjacent bones across the whole width of the suture. The early development of these bone-connecting fibres is illustrated in Fig. 2D in the suture of the zygomatic arch of a 250 mm. C.R. human fœtus (about 8 months old).

If it is remembered that during fœtal life the facial sutures are both sites of growth and sites of union between adjacent bones, it will be seen that with increasing age the function of growth gradually slows down and the function of union becomes consolidated and strengthened.

In previous papers (Scott, 1953, 1954) it was suggested that the cartilage of the nasal septum played an important role in the growth of the upper facial skeleton in the antero-posterior and vertical dimensions, acting as the means whereby the maxillary and circum-maxillary bones were separated from one another and from the anterior cranial segment (frontal and sphenoid) along the facial suture systems. The septal cartilage at birth extends from the cranial base to the maxilla in man, but in other animals from the cranial base to the premaxilla, its lower edge lying within the vomerine groove. This is so constructed as to allow the interstitially growing cartilage to slide in the groove without having to shift the position of the vomer (Fig. 5A). As a result it is the premaxilla which is directly acted on by the growing cartilage (Fig. 3A), and the premaxilla in its turn draws the maxilla downwards and forwards after it. In the same manner the maxillary bones exert a pulling action on the palatine bones which are drawn away from the cranial base and its extensions, the pterygoid plates. It follows that the greatest separating force is exerted at the premaxillary-maxillary suture, where this is present, and the least force at the pterygo-palatine suture.

Further Studies on the Cranial Base

Ford (1958) substantiates the statement that growth of the middle segment of the mid-line cranial base (pituitary fossa to foramen cæcum) is completed by the time of eruption of the first permanent molar (Scott, 1954). Furthermore, he states that growth of the cribriform plate of the ethmoid is complete by 2 years of age.

Fig. 3 (B and C) shows the growth sites along the mid-line cranial base just before birth (Fig. 3B) and the changes which have occurred by 7 years of age (Fig. 3C). During late fœtal life there are three growth sites between the pituitary fossa and the foramen cæcum. These are (1) the synchondrosis between the post-sphenoid element of the sphenoid body (carrying the greater wings) and the pre-sphenoid element (carrying the lesser wings), (2) the spheno-ethmoidal suture at the back of the cribriform plate area, and (3) the fronto-ethmoidal suture at the front of the cribriform plate area.

Fig. 3B shows that the midsphenoidal syn-

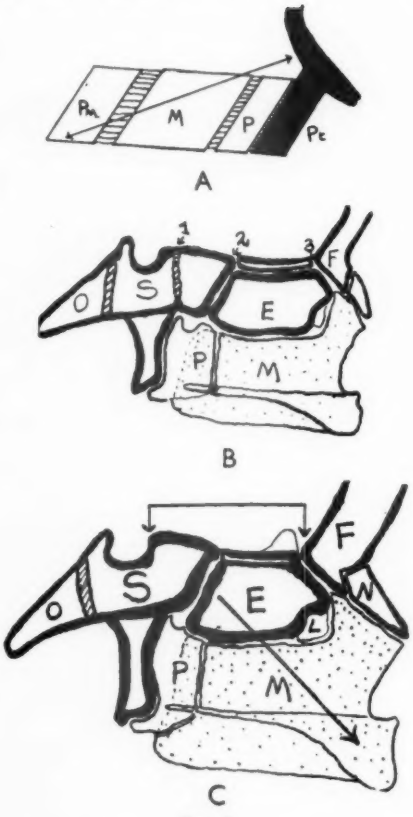


FIG. 3.

A, Diagram showing relationship between facial bones and sutures. Pm, premaxilla. M, maxilla. P, palatine. Pt, pterygoid plates.

B and C, facial and cranial bones at end of fœtal life and at 7 years of age. O, basioccipital. S, sphenoid. E, ethmoid. F, frontal. M, maxilla. P, palatine. L, lacrimal. N, nasal. 1, sphenoidal synchondrosis. 2, spheno-ethmoidal suture. 3, fronto-ethmoidal suture.

Arrow indicates position and direction of growth of septal cartilage.

chondrosis is in the same vertical plane as the palato-pterygoid suture. In man this synchondrosis is obliterated and the two parts of the sphenoid united at about the time of birth. In the *Macaca rhesus* monkey, however, it persists until the beginning of adult life. The spheno-ethmoidal suture together with the more laterally placed spheno-frontal sutures are in the same vertical plane as the palato-maxillary suture but, as has been previously shown (De Coster, 1951; Scott, 1954; Ford, 1958), growth at the sutures behind and in front of the cribriform plate has ceased by 7 years of age if not earlier. The slight amount of growth which takes place in the distance between the pituitary fossa and foramen cæcum (Fig. 3C) between 2 and 7 years (Ford, 1958) may be due to growth on the sphenoidal and frontal sides of these sutures, or, as is more likely, to a backward migration in the position of the pituitary fossa. This latter process certainly appears to take place in the anthropoid apes.

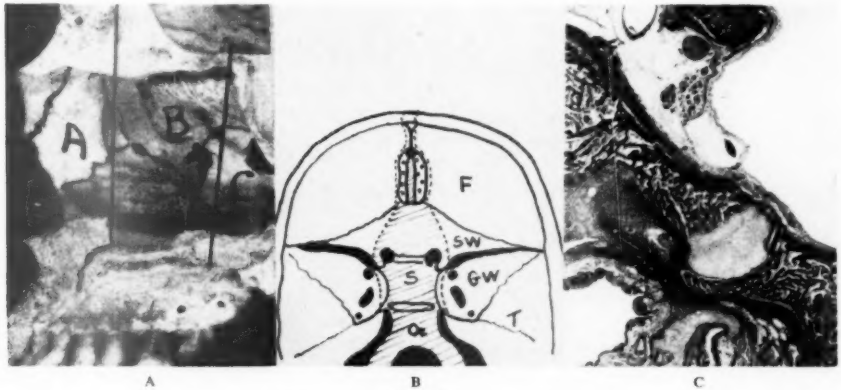
The time of union between the facial and cranial parts of the ethmoid across the cribriform plates is still uncertain but is almost certainly complete by 3 years of age (Ford, 1958). This means that there is probably no further growth in length of the facial ethmoid after this time although the perpendicular plate continues to extend into the cartilage of the nasal septum. Therefore, between 3 and 7 years of age the adult relationship between the body of the sphenoid, the cribriform plate, the facial ethmoid and the frontal bone has been established (Fig. 3C).

Growth of the Maxilla

During all this time and since early fœtal life, the growing cartilage of the nasal capsule and later the nasal septum has been thrusting the maxilla downwards and forwards allowing growth to take place between the maxilla and the circum-maxillary bones (the circum-maxillary suture system). It is still uncertain how much of this growth continues after about the 7th year and for how long.

It has been pointed out (Scott, 1956) that the positions of nasion and the posterior border of the maxilla as seen in X-rays are not reliable indications of circum-maxillary suture growth: the position of nasion because it migrates upwards by a process of surface growth at the fronto-nasal suture which does not involve any separation of the two bones (*see also* Ford, 1958); the posterior border of the maxilla because this, as seen in lateral cephalograms, is a free border (the anterior border of the pterygo-palatine fossa) which can extend backwards narrowing the fossa without, however, involving any growth at the more deeply placed palato-maxillary suture.

As measured from the incisive foramen to the transverse palatine (palato-maxillary) suture on the oral surface of the hard palate it would appear that this segment of the palate elongates throughout childhood by growth at the suture, but if the distance is measured on the nasal surface (Fig. 4A) the distance remains fairly constant after the 7th year and maintains a rather constant relationship to the length of the cribriform plate.



A B C

FIG. 4.

A, hard palate and nasal cavity showing relationship between roof of nasal cavity (cribriform plate) and hard palate (between nasal opening of incisive canal and transverse palatine suture). Note the difference in position of the nasal and oral openings of the incisive canal. A, B, C represent anterior, middle and posterior segments of nasal cavity.

B, diagram showing the sagittal suture system on the base of the skull. F, frontal. SW, lesser wing of sphenoid. GW, greater wing of sphenoid. T, temporal. S, body of sphenoid.

C, growth cartilage between body and greater wing of sphenoid in a 250 mm. C.R. human fœtus. × 4·5.

The different behaviour of the oral and nasal measurements is due to the forward migration of the incisive canal with descent of the hard palate (Fig. 4A), so that the oral measurement is not entirely an indication of sutural growth but rather of a change in the position of the oral opening of the incisive canal. It has been pointed out that further downward and forward growth of the maxilla after about the 7th year (when the size of the orbital cavity has reached about 95% of its adult size) would involve surface deposition on the floor of the orbital cavity (orbital plate of the maxilla). This in turn would, if at all extensive, result in a covering in of the infra-orbital groove extending the infra-orbital canal backwards to the pterygo-palatine fossa. This does not, however, usually happen and in those cases where it does occur the roof of the bony canal is very thin.

The available evidence, therefore, would seem to indicate that, allowing for individual variation, there is little growth at the circum-maxillary sutures during the second decade of childhood (10–20 years), but the preliminary work of Björk (1955) based on the use of amalgam implants indicates that the problem is still open and that some of the statements made by the present author on this matter have been perhaps too dogmatic.

Growth in Width of the Skull

At birth the skull and face can be divided into left and right halves along the mid-sagittal suture system (Scott, 1957). As seen from the frontal aspect of the skull this consists of the interparietal and interfrontal sutures of the vault; the internasal suture; the suture between the two maxillary bones and its extension on the palate as the mid-palatal suture; and the mandibular symphysis. As seen on the floor of the cranium, the sagittal suture system is more complex. Behind the foramen cæcum it divides to run on either side of the mid-line cranial base (Fig. 4B). At this time the great wings of the sphenoid are united to the body of the bone by a mass of cartilage (Fig. 4C). During fœtal life this cartilage and that of the roof of the nasal capsule play an important role in determining the growth of the sagittal suture system correlated with the rapidly growing brain which, however, exerts its main influence on the bones of the cranial vault, and has little if any effect on the growth of the cranial base. At about the time of birth, the greater wings of the sphenoid unite with the body, and during the first year the two halves of the frontal unite (except in the rare cases showing a metopic suture) as do the two halves of the mandible. By the end of the first year only the interparietal, internasal and intermaxillary sutures remain of the mid-line sagittal suture. By this time the width across the bridge of the nose (dacryon to dacryon) has reached 75% of adult size and further growth is by surface deposition at the medial wall of the orbital cavities rather than by growth at the internasal suture (Ford, 1958). As this measurement includes the frontal processes of the maxillary bones it would seem that there is little if any growth at the suture between them and the nasal bones after the first year (Fig. 5B).

After the first year both the frontal and the sphenoid bones are continuous from one temporal fossa to the other, and together form the upper and lower halves of a bony ring which, with its extensions the pterygoid plates, bounds and supports the facial skeleton. This fronto-sphenoidal ring grows by surface deposition associated with internal resorption (Fig. 5B).

The relationship of the palatine tuberosity to the notch between the pterygoid plates is interesting in this respect (Fig. 5C). By this interlocking mechanism growth between the greater wings and body of the sphenoid during fœtal life is correlated with growth at the mid-palatal suture. With union between the parts of the sphenoid, the pterygoid plates no longer undergo a process of bodily separation and this will limit to a considerable extent the amount of growth that can occur between the palatine bones at the mid-palatal suture. Growth in width and height of the posterior nares after birth would seem to be almost entirely a matter of bone resorption correlated with bone deposition (Fig. 5C). In the upper ethmoidal part of the nasal cavity this is certainly the case after the union between the facial and cranial elements of the ethmoid has taken place. There is surface deposition on the orbital side of the facial ethmoid associated with pneumatization on the nasal side, producing the ethmoidal air sinus system.

Alveolar Bone Growth and Tooth Movements

Tooth movements in the jaws can be divided into three categories:

(1) Separation movements between the developing and growing tooth germs correlated with the growth of the overlying oral mucous membrane (gum) to which they are attached by their follicular sacs (Wasserfallen, 1954).

(2) The movement of active eruption within the follicular sacs produced by the growth of the pulp expanding between the calcified shell of the tooth crown and the base of the follicle (Scott, 1948).

(3) Migration of the upper and lower dentitions through the alveolar bone. It is this later type of movement which we discuss here.

That part of the alveolar bone which is growing by surface deposition lies beneath the muco-

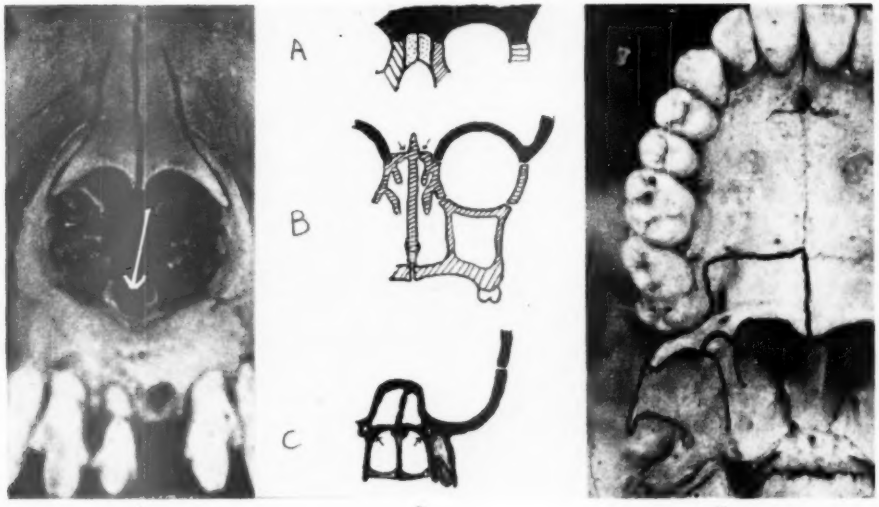


FIG. 5.

A, vomerine groove in a dog.

B, diagram showing relationship of frontal (A and B) and sphenoid (C) to the bones of the facial skeleton. In B arrows indicate place of union between facial and cranial parts of ethmoid at cribriform plate; in C arrows indicate position of growth cartilage between body and greater wings of the sphenoid.

C, showing the relationship of the palatine bone to the pterygoid plates.

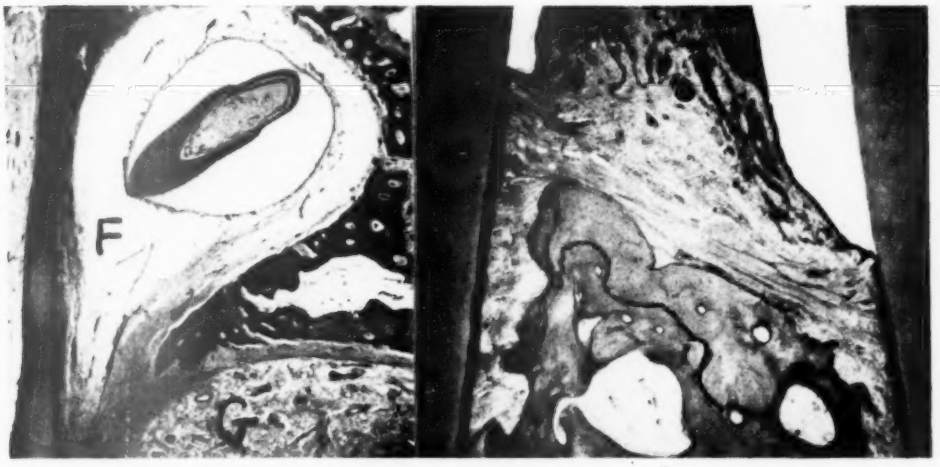


FIG. 6.

A, developing upper incisor in its follicle in a 6-week-old kitten. × 27. F, follicular sac. G, gum. Note attachment of follicle to gum via gubernacular cord and the deep osteogenetic layer of gum adjacent to alveolar bone.

B, showing attachment of gum to adjacent teeth (transeptal fibres) and relationship to growing alveolar bone. (By courtesy of Dr. H. J. J. Blackwood.) × 22.

periosteum of the gum, the deeper layer of which is osteogenetic (Fig. 6A).

To the overlying gum are attached the follicles of the developing teeth: directly in the case of the deciduous teeth; through the common molar gubernacular cord in the case of the permanent molars; and through their individual gubernacular cords in the case of the successional permanent teeth (Fig. 6A). The teeth which have erupted and are in occlusion are attached to the gum at their necks through the gingival and transeptal fibres (Fig. 6B). As new bone is laid down by the deeper osteogenetic layer of the gum the overlying gum tissue is translated in the direction of alveolar bone growth, which is upwards, forwards and outwards in the lower jaw, and downwards, forwards and outwards in the upper jaw. As the bone grows both the developing and erupted teeth are carried in the direction of its growth in virtue of their attachment to the gum. The so-called "mesial migration" of the dentition is therefore only one aspect of a three-dimensional growth movement involving the whole dentition. In human dentitions the predominant direction is vertical, and it is this vertical growth of the alveolar bone, carrying the teeth with it, which maintains them in occlusion as the mandible in its growth is separated from the upper facial skeleton. In some cases the amount of growth necessary to maintain occlusion, especially in the molar region, is quite extensive (Fig. 7).

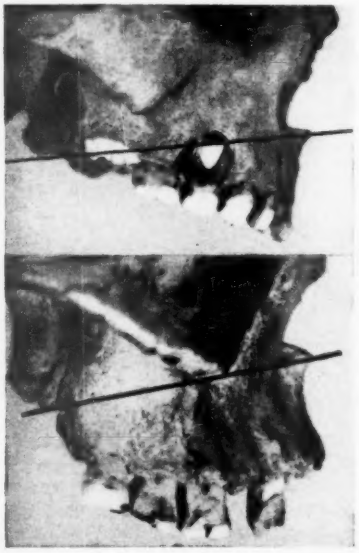


FIG. 7.—To show vertical growth of alveolar process in upper jaw. A, 5-year-old child. B, adult.

The Relationship of the Mandibular Ramus to the Upper Facial Skeleton

The width of the ramus of the mandible (condyle to coronoid process) is correlated with the length of the zygomatic arch as measured from the anterior edge of the articular eminence to the lower end of the zygomatico-maxillary suture (usually marked by a tubercle) and is related to growth at two suture systems:

(1) The coronal suture system which includes the suture of the zygomatic arch between the temporal and zygomatic bones and is regulated in its growth by the spheno-occipital synchondrosis (Scott, 1954).

(2) The posterior, vertical limbs of the circum-maxillary and cranio-facial suture systems in the pterygo-palatine fossa.

The coronal suture system is a site of growth until adult life, while the pterygo-palatine sutures probably cease to play any significant role after the end of the first decade.

The zygomatic arch also probably extends by a process of resorption behind and deposition at the front of the maxillary zygomatic process, but in man this is probably limited in amount.

Growth at the condylar cartilage thrusts the mandible downwards and forwards from the glenoid fossa. The forward element in this growth process would carry the anterior edge of the ramus beyond the vertical plane of the anterior surface of the temporal fossa, which coincides with the anterior edge of the temporal muscle, if there did not occur at the same time a process of resorption along the anterior edge of the ramus where the anterior fibres of the temporal muscle are attached. Resorption of bone at the anterior edge of the ramus therefore takes place in order to maintain the proper relationship between the zygomatic arch and also the origin and insertion of the temporal muscle during the period of facial growth. It is not primarily related to the development of the dentition as is shown by its occurrence in edentulous animals, in children showing complete anodontia, and by the fact that the anterior part of the ramus may overlap the third permanent molar on its outer side in whole or in part (Scott, 1958).

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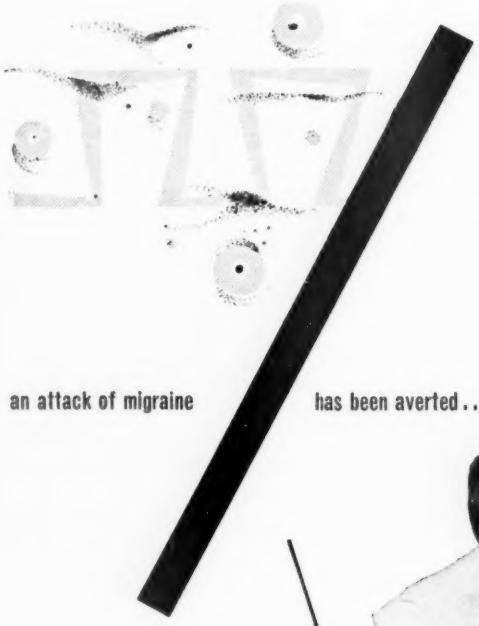

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Section of Psychiatry

President—Professor E. STENGEL, M.D., M.R.C.P.

Meeting
December 10, 1957

The Follow-up of Children with Tuberculous Meningitis with Special Reference to Psychiatric and Neurological Aspects [*Abstract*]

By JOHN LORBER, M.D., M.R.C.P.
Sheffield

A COMPREHENSIVE analysis of the long-term results of treatment of tuberculous meningitis was presented on the basis of 100 consecutive surviving children treated at the Department of Child Health of the University of Sheffield and who have been observed for three to ten years. Routine clinical and radiological examinations at regular intervals were supplemented by annual intelligence tests, repeated electroencephalography, and audiometry. Reports from schools were obtained and were compared with the children's previous records where applicable.

78 were free from all physical defects and 12 had considerable neurological residual lesions. The I.Q. of 7 children was 120 or more after recovery and of 6 it was less than 50. The vast majority (67) had an I.Q. of 81–110. The severely retarded children were all 2 years of age or less at the time of their meningitis. The scholastic progress of 45 was good or average, but 35 were dull. The behaviour of children with an I.Q. of 70 or over was normal in 88. Major personality disorders were present in 2. Sexual precocity occurred in three girls. In 41 children the EEG failed to return to normal, although 16 of these had no neurological or mental changes at any time. Intracranial calcification developed in 45 children.

President—ELIOT SLATER, M.D.

Meeting
October 14, 1958

Dr. ELIOT SLATER delivered his Presidential Address on **The Problems of Pathography.**

Meeting
November 11, 1958

Psychiatric Morbidity in an Urban Group Practice [*Abridged*][1]

By MICHAEL SHEPHERD, D.M., MICHAEL FISHER, M.B., LILLI STEIN, M.A., Ph.D., and W. I. N. KESSEL, M.R.C.P., D.P.M.
London

INTRODUCTION

MUCH of the work bearing on the epidemiological aspects of mental disorder has been related to patients in institutions, where the population is conveniently circumscribed for the purposes of investigation. These studies have, in consequence, been largely concerned with the major psychiatric disorders from which the patients principally suffer: the functional psychoses, the senile psychoses, the epilepsies and mental deficiency. The early studies of mental illness outside hospital were conducted in the main by investigators interested in the genetic background of the same conditions. For an adequate assessment of the nature and amount of mental illness in the community, however, there is an additional need for systematic study of the minor psychiatric disorders: the neuroses, the abnormalities of personality, the behaviour disorders and the psychophysiological disturbances. Here hospital populations have proved less useful; only a minority of the individuals

[1]Many of the data have had to be omitted and will be published elsewhere.

suffering from these disabilities require admission and though an uncertain proportion may be seen as out-patients they do not necessarily attend the hospital psychiatric departments.

Research into mental ill-health in the community has been greatly stimulated by the methods employed by public health authorities and epidemiologists in surveys of general morbidity. Attempts have been made to investigate groups of people whose experience of ill-health is readily accessible, e.g. military personnel, factory workers or members of insurance schemes. With improved techniques it has also proved possible to study more representative samples of a population, as in the well-known Eastern Health District of Baltimore. In work of this type there is one medical agent, namely the general practitioner, whose unique position between the hospital and the community renders his experience of particular value provided that it can be recorded systematically. For this reason the general practitioner's role in the study of morbidity has now gained widespread recognition in this country. Since the introduction of the National Health Service several studies of patients' needs, doctors' services and individual diseases have been undertaken by the Social Medicine Unit of the Medical Research Council, the General Register Office and the College of General Practitioners.

The bulk of this important work, however, has been concerned only indirectly with the problems in which the psychiatrist takes a special interest. At the present time a dearth of reliable quantitative information hampers the value of most activities in the field. The links between general practitioners and psychiatrists have been strengthened by the development of domiciliary consultations but there remain wide differences in general practitioners' referring habits to hospital. There is also considerable variation in the size of the general practitioner's psychiatric case-load according to the reports which have appeared from individual doctors who have analysed and commented on their own clinical experience (Watts, 1956). In Lord Taylor's opinion (Taylor, 1954) the neuroses account for 5–10% of the general practitioner's new cases; the working party of the Council of the College of General Practitioners (1958), on the other hand, refers to a "generally accepted figure . . . in the region of 30%" and some practitioners have exceeded this estimate. Part of the explanation for this diversity of opinion may lie in true differences of prevalence related to the effects of geographical and social factors or to the selection of particular doctors by their patients. It is equally apparent that the attitudes of the general practitioners and their readiness to make a psychiatric diagnosis also play a role in the identification of psychiatric cases. In his study of eight practices Logan (1953) has made this point explicitly to account for the high rate of psychiatric morbidity recorded by one of the practitioners who took special pains to make a note of psychoneurotic conditions. A third source of variation lies in the different systems of classification which have been employed.

With these factors in mind we initiated a socio-medical investigation into some of the psychiatric problems of a population defined by reference to one group practice in South-East London. Our particular interest was in the nature and amount of mental ill-health conspicuous to the practitioners during one year and no attempt was made to seek out people who did not consult them.

The Practice

The four practitioners (Dr. M. Fisher, Dr. I. Fisher, Dr. C. Benn and Dr. L. Morgan) hold eleven surgeries weekly. Two doctors in rotation are present at each surgery and two undertake the home visits. An appointment system and a secretary help to ensure that every doctor-patient contact is entered on the patient's medical record. The medical records have always been kept carefully for the purposes of administration and efficient doctoring, particularly as more than one doctor may see the same patient.

Many additional activities have been developed with the aim of providing a fully comprehensive service "from the cradle to the grave", with an increasing emphasis on preventive medicine (Chalke and Fisher, 1957). The stress laid on the patients' social background and their everyday problems has gone with an appreciation of the psychological components of illness but none of the four doctors has had special psychiatric training. Their policy has been to treat the mentally ill patient within the practice whenever possible and to request the help of psychiatric colleagues when necessary.

Method

The "population" studied was a 20% random sample of the practice list of approximately 9,000 registered patients. The illnesses were studied for one risk-year, March 1956 to February 1957. For practical reasons the sampling was done by random selection of initial letters of surnames; all patients who were registered before the risk-year and whose surnames began with one of *six* letters of the alphabet were included. For the whole 20% sample basic data on age, sex, marital state, registration in the practice, consultations, &c., were transferred from N.H.S. cards to

punch cards. The patients covered by these six letters were subdivided into a four-letter group (13⅓% of the practice) about whom medical information was obtained from the general practitioners and a two-letter group about whom the medical data were abstracted directly from the N.H.S. cards and other practice records. The medical information about the two-letter sample will not be discussed further in this paper. For a sub-section further social and demographic data were obtained by interview and questionnaire. Since most of the questionnaires were administered to patients in surgery during the summer following the risk-year this group did not constitute a random sub-sample but was weighted by patients attending surgery, particularly those with young children. It amounted to one-half of the sample and yielded additional data for persons in the whole household (including non-patients) regarding occupations, job history, housing, duration of residence in house, &c. The three units of analysis which were used for the social data were: (1) the patient —represented by the N.H.S. card; (2) the patient group—represented by one address for a group of cards; (3) the whole household—for the section covered by the questionnaire.

The medical data relate to "attenders", i.e. patients who had made at least one medical consultation in the risk-year. The unit of work analysed was the consultation. It was not considered possible to assess conspicuous psychiatric morbidity without reference to the general pattern of morbidity in the practice. Medical data were obtained therefore about every adult patient (aged 15 or over) in the four-letter sample at discussions during May to July 1957 between the general practitioners and one of us (W. I. N. K.). The N.H.S. record cards were examined and details were collected about the patients' illnesses during the year and their significant illnesses in the past. Further information about these patients for the preceding and subsequent years was abstracted directly from the record cards. The general practitioner was asked about overt psychiatric illnesses and the presence or absence of psychiatric components of other illnesses during the year (*see below*). Where there was no conspicuous psychiatric disability the practitioner was invited to comment on any abnormal features of personality.

Socio-economic Features

In view of the importance of the social correlates of ill-health it was necessary to secure social and demographic information about the population at risk. An outline of some family and socio-economic characteristics demonstrates that the sample whose morbidity was studied was not made up of an abnormal or extraordinary group of people in respect of these features.

There were 911 adults and 282 children in the four-letter sample—539 males and 654 females; over half had been in the practice since before 1949. The age composition differed somewhat from that of South-East London generally. Children under 15 formed nearly one-quarter of the sample; there was also some excess of women aged 30–44 years, but a significant deficit of single men at all ages—perhaps understandable in view of the practice's special facilities for babies and toddlers.

The average size of patient-group at one address was 2·1 patients, and over 40% of addresses had only 1 patient. In the households covered by questionnaire the average patient-group was larger, 2¾ patients; the whole household averaged 3½ persons, slightly larger than the average for England and Wales. A high proportion (nearly 60%) of the households contained children under 16 years. An indication of the stability of these families is provided by the fact that less than 2% of them had migrated into the district during the previous two years and 42% of the families had lived in the same house for ten years or longer.

The households covered by questionnaire had a higher proportion of men in social class 3 and lower proportions in classes 4 and 5 than the average for England and Wales. The occupational stability of the men is indicated by the fact that nearly one-fifth had been in the same job for fifteen years or longer. The number of earners in relation to all members of the household averaged 0·44, a figure very similar to the average for England and Wales. These earners were mainly men and single women; the married women were mostly housewives, and those who did work outside their homes were as commonly in part-time as in full-time employment.

General Morbidity (excluding Psychiatric Illness)

(1) *Consultations.*—Of the whole sample, 70% made at least 1 consultation during the year, and these attenders averaged 5¾ consultations each. Among children under 15, the attendance rate was rather higher and did not differ markedly between the sexes. Among adults, however, the percentage of men who attended (67%) was lower than that of women (75%), and the average number of consultations for male attenders (5¾) was also a little lower than for females (6¼). It is interesting to note that the percentage of patients attending at least once was fairly steady in all adult age-groups but the average number of consultations for adult attenders increased with age.

There were very few significant trends of attendance in relation to social and family features. Length of time in the practice, size of patient-group and occupational class showed no association with attendance. Job duration, perhaps surprisingly, did show an association; among the men who had been in their jobs for an intermediate period of time (three to eight years) there was a significantly high percentage of attenders. For the women, marital state, child status and employment did not show any strong connexion with frequency of attendance. There was a slightly lower average of consultations for married women than for single; within the married group the housewives had fewer consultations than either the full-time or the part-time employed.

(2) *Illnesses.*—We adopted the working definition of illness proposed by Backett *et al.* (1953), namely "a disturbance of a patient's health that is reflected in at least one consultation". All illnesses were assigned to appropriate systems in the WHO International Classification of Diseases. By this method the illnesses for which the adult patients consulted their practitioners were found to be similar to those in other general practice studies. Patients with respiratory illnesses consulted the doctors most frequently; 41% of adult attenders suffered at least one such illness during the year. Locomotor disorders (31%) ranked second and abdominal illnesses (23%) third. Dermatological, ophthalmic and aural illnesses were the other large groups among both men and women. In addition, genito-urinary disorders formed a large group for women (22%), though not for men (4%). A smaller excess among women was noted for illnesses referable to the central nervous system and for overweight. Examination of the age-distribution of illnesses showed a number of trends. Skin disorders, for example, affected higher proportions of both sexes under the age of 20; abdominal illnesses were recorded most frequently among men aged 30–44; complaints of debility, for both sexes, were most frequent in the middle years of life.

The availability of four doctors went some way towards offsetting the bias of a self-selected group of patients. Comparisons of the adults consulting each of the four general practitioners, however, indicate that there was some self-selection of patients within the group practice. There were several differences in the age-sex composition of the adults who attended each doctor. The female doctors averaged a higher number of consultations for both men and women patients. Further, the morbidity pattern among patients of individual doctors displayed differences suggestive of self-selection.

Psychiatric Morbidity

To assess the prevalence of psychiatric ill-health it was necessary to arrive at operational criteria of morbidity. The use of the WHO International Classification of Diseases underestimates psychiatric morbidity since some of the illnesses classified in symptomatic terms include a proportion of psychological disorders; it is also difficult to take account of the psychiatric aspects of established physical disease with this method of classification.

Two other methods of classification were therefore employed. On the basis of predetermined criteria we allocated each illness to one of three groups. Group 1 comprised the psychoses and all illnesses where the patient couched his complaint in psychological terms. Illnesses expressed in somatic terms were divided into those in which the symptoms could not reasonably be ascribed to physical disease (group 2) and those which were consequent upon pathological changes (group 3). This classification is used here only to discuss the reasons for consultation.

The principal approach to an estimate of psychiatric morbidity was based on the general practitioner's medical judgment. Though observer error and memory factors must affect such an estimate, this judgment represents the best available knowledge of the patient and his circumstances. Prior agreement had been reached upon the criteria of psychiatric disability to be adopted. Psychosis and mental deficiency, though easily identified, are encountered infrequently in the surgery. Experience suggested that most of the other psychiatric disabilities presented in three ways. Some patients displayed psychological symptoms such as anxiety, depression, irritability or nervousness. Others had somatic symptoms which the practitioners could not explain adequately by physical illness: headache, insomnia, palpitations and menstrual disturbances were common examples. Finally there were patients whose psychological reaction to indisputable physical illness was in some way abnormal. In addition, there were a number of patients whom the general practitioners were not inclined to regard as having suffered from a psychiatric disability but whose personalities they considered to be in some way abnormal.

(1) *Prevalence rates, age and sex.*—Of the 911 adults at risk in the four-letter sample 620 attended during the year—253 men and 367 women. The general practitioners identified 86 patients, 28 men and 58 women, as having presented a conspicuous psychiatric disability. The one-year-period prevalence rate for persons with conspicuous psychiatric disability was thus 9% of all registered patients (11% for women

and 7% for men). Another 5% of registered patients were considered by the general practitioners to have displayed abnormal personality traits independent of the presenting illness. In this group also women exceeded men.

The rates for women showed some increase in middle age but there was no age trend for men. (With the WHO classification men also displayed a higher rate in middle age.) Fry (1957) reports similar findings but they differ from most hospital reports which suggest an association of neurosis with the younger age groups.

The need to specify carefully the criteria on which any estimate of psychiatric morbidity is based may be illustrated by a comparison of the different prevalence rates which could be derived from the same data. 8% of adult attenders had psychological symptoms at some time during the year. Inclusion of all patients who had had an illness without obvious physical cause would have inflated the estimate to 38%; with the addition of patients with "psychosomatic" or "stress" disorders the rate would have risen to more than 50%. This figure would still have left out those patients whose psychiatric disability was expressed as an elaboration of the symptoms of established physical disease.

(2) *Illnesses.*—Only 3 of the 86 patients with conspicuous psychiatric morbidity exhibited psychotic symptoms during the year; there were also 2 mental defectives. It was not possible to make formal psychiatric diagnoses for the remainder but anxiety characterized the largest group; hysterical reactions, depression and hypochondriacal reactions were also observed. Among these patients there was a higher prevalence of complaints loosely referable to the central nervous system—headache, giddiness, &c.—than among the generality of attenders. Otherwise the distribution of physical illnesses was the same as for all attenders except for an excess of abdominal and orthopædic illnesses among the women.

9 patients were referred to a psychiatrist during the year. They constituted 1·5% of all attending patients and 10% of the identified "psychiatric" patients. These 9 people included the 3 psychotic patients but it was not possible to elucidate the factors determining referral for the other 6 whose illnesses were similar in form to those of several patients who were not referred to hospital.

Of all patients with a definite history of psychiatric illness before the risk-year only about one-half were considered to have displayed psychiatric disability during the year. By the criteria adopted for detection, therefore, approximately one-half of their illnesses had remitted. During the subsequent year three-quarters of the "psychiatric" patients made the same complaints as in the risk-year; one-eighth of the patients either did not attend or made no consultations for the same condition that had led to their identification; no assessment could be made about the remaining eighth.

(3) *Consultations.*—62% of the consultations were with female patients, 38% with males. 71·8% of consultations were devoted to physical disease. In 6·8% of consultations the patients had psychological symptoms; 21·4% of consultations were concerned with illnesses without apparent physical cause.

The average annual number of consultations for the "psychiatric" patients was 9·7, nearly double that of the remaining patients (5·1). A high attendance rate was also recorded in the preceding and subsequent years. One-quarter of the group attended very often during the risk-year and so contributed unduly to the high average. Women (10·1) attended more frequently than men (8·8); this sex difference did not obtain for the other patients.

(4) *Social factors.*—The social factors which were measured did not distinguish patients with conspicuous psychiatric morbidity from the whole population. However, the general practitioners regarded disturbed family relationships as ætiological factors in the illnesses of 20% of these patients.

Conclusion

The social and general medical characteristics of the sample indicate that it was not composed of highly selected or unusually sick people. From the sociological standpoint they seemed to be ordinary families, stable in their homes and jobs; a high proportion had young children. Most were of the skilled working-class and had social contacts in the area and relatives near by. From the medical standpoint they seemed to come to their doctors about as often, and for the same kinds of illness, as the patients in other general practices from which findings have been published.

The one-year-period prevalence rate for adults with conspicuous psychiatric disability was 9% of the registered population; the rate for women exceeded that for men. These people attended more often than other patients but presented a similar pattern of consultations for physical disease. They were not remarkable in their social characteristics. Only 10% of patients

with conspicuous psychiatric ill-health were referred for specialist opinion.

While the findings from one group practice do not permit of generalization the available evidence does not suggest that an overestimate of conspicuous psychiatric ill-health has been provided. If it is of this order of magnitude in the community it should claim more attention from both the psychiatrist and the general practitioner.

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Meeting
December 9, 1958

The Role of Stress in the Ætiology of Pyschosomatic Disorders
[*Abridged*]

By LINFORD REES, M.D., M.R.C.P., D.P.M.

London

Definitions

The term *stress* has a varied history and would undoubtedly be regarded by Ogden and Richards (1931) as a nomad in view of its changing meaning and usage throughout the centuries. Judging by current usage of the term it would seem that its wandering tendency has not yet ceased.

Stress, used as a noun, probably originated as an aphetic form of distress and in the fifteenth century was used to denote hardship, adversity and sometimes to describe forces or pressures applied to a person for purposes of compulsion or extortion.

In physics the term stress has a precise meaning and refers to a force which, when applied to a material, produces a change in shape which is referred to as strain. In the early nineteenth century stress was used synonymously with strain and was often used to denote strain on bodily and mental functions. Since this time the word stress has been applied to external forces or stimuli as well as to the effects of such on the organism and sometimes to the point of interaction between them.

In biology and medicine the term stress is of comparatively recent introduction and has been variously applied to external stimuli as well as their effects on the organism.

Among the current uses and applications of the word stress is that of Stewart Wolf (1950) who uses the term in a roughly similar fashion to its use in physics. He regards stress as the external stimulus or force which is strain-producing or potentially strain-producing to the person to whom it is applied. Anything may be considered a stress if it threatens the biological integrity of the organism, whether directly by its physical or chemical properties or indirectly because of its symbolic meaning. Harold Wolff (1952) uses the term stress as the internal resisting force brought into being in the organism by interaction with the environment; Selye (1957) to denote a specific syndrome occurring in the body in response to certain agents which are designated stressors.

In general medicine and psychiatry the term stress is commonly used to denote various psychosocial situations which tend to produce disorganization of behaviour, including physical and mental illnesses. Responses of different individuals to potentially stressful psychosocial situations show considerable variation. The response may be apt and adaptive or it may be inept or maladaptive, the latter sometimes taking the form of physical or mental illness. The precise relationships between the psychosocial situations which are potentially stressful and their effects on the organism on the one hand, and the various stressor agents described by Selye (1957) and their effects on the organism on the other, require further research for their elucidation.

A convenient definition of stress would be any stimulus or change in the external or internal environment which disturbs homeostasis and which, under certain conditions, can result in illness.

The terms stress and stressor are really abstractions and are only meaningful in relation to their effects on the organism and it might be better to use stress adjectivally as suggested

by Vickers (1958) to the three distinct processes involved in reactions to stress, namely:

(1) The forces, stimuli, changes, conditions or situations which are stressful.

(2) The processes whereby (1) produce their effects on the organism.

(3) The changes in the organism resulting from (1), including behavioural, emotional, physiological, biochemical and structural changes.

Psychosomatic disorder.—I propose to use this term for those physical illnesses in which psychogenic as well as physiogenic factors are ætiologically important. I am including under this rubric only those disorders in which emotional and other psychogenic factors play a predisposing or precipitating role, demonstrable clinically or experimentally. In the majority of disorders so defined, genetic and constitutional factors are also important.

Particular reference will be made to investigations I have carried out on the following disorders: asthma, vasomotor rhinitis, hay fever, urticaria/angioneurotic œdema, peptic ulcer and thyrotoxicosis. The consideration of the role of stress in the genesis of psychosomatic disorders brings us into the complicated field of ætiology. Theoretically there are innumerable possible causes which may be considered in relation to any event including illness. In medicine it is clearly unprofitable to consider all possible causes in illnesses as only some will be relevant in clinical practice and therefore the problem resolves itself into a search for factors in the environment or in the individual which are relevant and causal. As physicians we are particularly interested in the extent to which these forces can be controlled or modified. Some causes will be essential, without which a disease cannot develop, but there will be other factors which will have as much claim to be a cause as they determine the actual manifestation of the essential cause as a disease. For example, the tubercle bacillus is essential for the development of the disease tuberculosis, but its presence in the body is in itself insufficient for the development of the disease and certain other conditions have to be present for this to happen. It is therefore not permissible to say that the tubercle bacillus is *the* cause of tuberculosis but that it is *a* cause or *a* factor. It may properly be designated the *essential* cause and the conditions which are necessary for its manifestation as the *sufficient* causes as suggested by Woodger (1956).

In considering the role of stress in the ætiology of psychosomatic disorders it is first necessary to establish a statistically significant temporal relationship between the occurrence of stress and the manifestations of the disorder and then to determine whether the stress comes under the category of essential causes or sufficient causes.

Concepts of specificity.—During recent decades a number of theories alleging specificity in psychosomatic relationships have been postulated and greatly elaborated. Specific factors in the environment and in the individual have been claimed to be causally relevant in the development of psychosomatic disorders; for example, French and Alexander (1944) claimed that the asthmatic attack occurs when there is a separation or a threat of separation from the mother; Miller and Baruch (1948) describe specific parental attitudes in the ætiology of asthma in children; Lidz and Whitehorn (1950) report specificity in the type of psychosocial stress at the onset of thyrotoxicosis, namely a break of important interpersonal relationships; Wittkower (1953) relates outbreaks of urticaria to a loss or threatened loss of love; Lindemann (1950) stresses the importance of bereavement and grief reactions in ulcerative colitis and so on. Specificity in attitudes in various life situations for different psychosomatic disorders is reported by Grace and Graham (1952); specificity of personality type or profile for each psychosomatic disorder is put forward by Flanders Dunbar (1946) and Halliday (1948). Others claim that specificity of emotional changes and physiological concomitants occurs in different psychosomatic disorders (Alexander, 1943). Theories of specificity relate largely to a specificity of stimulus which allegedly produces specific psychophysiological responses and specific psychosomatic disorders.

The validity of these claims, together with the possible role played by various stresses at the onset and during the course of illness of different psychosomatic disorders will be considered in the light of the findings carried out by the author in the following groups of patients: asthma 800 patients, vasomotor rhinitis 68 patients, hay fever 50 patients, urticaria/angioneurotic œdema 100 patients, peptic ulcer 40 patients, thyrotoxicosis 40 patients and various control groups matched for age and sex distribution with the psychosomatic groups totalling over 400 subjects.

Types of Psychosocial Stress at the Onset

It was found that stressful life situations preceded the initial attack in 12% of asthmatic children, 36% of asthmatics between 16 and 45 years of age and 46% of those having onset after 45 years; vasomotor rhinitis in 30%, hay fever in 10%, urticaria/angioneurotic œdema in 51%, peptic ulcer 47% and thyrotoxicosis 45%. Apart from asthmatic children and the hay fever group the occurrence of stress preceding the onset was significantly higher in all psycho-

somatic groups than in the corresponding control groups.

In all forms of psychosomatic disorder and at all ages and in both sexes, a diversity of stressful life situations was found, with no evidence of any specificity for each particular disorder. Some of the stresses were sudden, occurring at a definite point in time, e.g. bereavement, accidents and illnesses to a loved person and various traumatic experiences of the patient. Other stresses operated over a longer period of time; such as family and marital difficulties, work and financial problems, sex conflicts and a variety of miscellaneous conflict situations. The type of psychosocial situation which is potentially stressful and relevant in development of psychosomatic disorders varies according to the age of the individual. In asthmatic children, parental lack, faulty parental attitudes, particularly those of rejection, overprotection or perfectionism are especially important, whereas in elderly asthmatic patients, stresses arising from adjustment difficulties following retirement or death of a spouse were found to be of particular importance.

Stressful Life Situations Associated with the Precipitation, Recurrence or Exacerbation of Attacks During the Course of the Illness

The types of life situation associated with the occurrence of attacks during the course of the illness were similar to those associated with the onset. All varieties of stressful situation were found in each disorder with no evidence of specificity of life situation in the precipitation of attacks during the illness. The life situations relevant in this connexion were varied and do not lend themselves readily to classification but the following constituted the main groups: (1) Bereavement of a loved person. (2) Threat to a loved person by illness or accident or other cause. (3) Marital and family problems. (4) Work and financial problems. (5) Conflicts relating to individual needs, including sex drives, ambitions, prestige, status, &c.

We therefore find no evidence of any specificity in the type of stressful life situations, either at the onset or in association with the occurrence of attacks during the course of the illness. The common factor appears to be that which is perceived by the individual as a threat to security in its widest sense.

Emotional and Other Precipitants of Attacks

The study of correlations between stressful life situations or emotional changes and attacks is facilitated when the manifestations of the illness occur at a definite point in time and are readily observable by the investigator, as in asthma, vasomotor rhinitis, hay fever and urticaria/angioneurotic œdema. In the case of peptic ulcer and thyrotoxicosis it is less easy to study such relationships. In Table I the percentage incidence of emotions, allergic factors and infections as precipitants of attacks during the course of the illness in the first group of disorders is given. It will be seen that emotional changes can precipitate attacks in from one-third to three-quarters of patients but that other precipitants operate also in the majority of patients. It was found that a variety of emotions could precipitate attacks or produce exacerbations in every disorder and there was no evidence at all of any specificity of emotional change for this disorder. In fact many different kinds of emotional change were found to be capable of precipitating attacks in all disorders, the most common being anxiety, anger, resentment, hostility, humiliation, depression and sometimes even joy and elation. The suppression or bottling up of emotions was found to be more important than the type of emotion experienced.

TABLE I.—EMOTIONAL FACTORS AND OTHER PRECIPITANTS OF ATTACKS

Disorder	Emotions	Allergy	Infections
	%	%	%
Asthma	74	36	38
Vasomotor rhinitis	57	56	57
Hay fever	36	100	0
Urticaria / angioneurotic œdema	68	35	15

A large number of *Personality Attributes* were rated on a three-point scale in various psychosomatic disorders. It was found that there was a general similarity in the incidence of various personality traits and between various psychosomatic disorders rather than any tendency for specific personality types or specific constellations of personality traits in different disorders. There was, however, a tendency for certain traits of personality to be significantly higher in some psychosomatic disorders than their corresponding control groups, particularly the following: anxious, sensitive, obsessional, meticulous. These tended to be higher in all psychosomatic disorders rather than to be specifically related to any particular condition.

Grace and Graham (1952) claimed that there were *Specific Conscious Attitudes* to the precipitating situation for each psychosomatic disorder and that there were specific physiological changes associated with each attitude. For example they state that urticaria occurred when the individual saw himself as being restricted and when he felt unable to retaliate or find a solution to his problem; that eczema occurred when the individual felt he was being interfered with or prevented from doing something and was unable to think of any way of dealing with the frus-

tration; vasomotor rhinitis and asthma were said to be associated with similar attitudes, viz. when the individual faced with a situation wishes that he had not to do anything about it, that is would like to deal with it by excluding it; duodenal ulcer when the patient was seeking revenge and so on. Grace and Graham (1952) based these claims on rather small groups of patients which may not have been representative samples of the disorders and their claims have not been confirmed by other investigators.

In the investigation of the psychosomatic groups referred to in this paper, consisting of over 1,000 patients, I found that only a small proportion of patients with each disorder showed the special attitudes described by Grace and Graham (1952); many other attitudes also occurred in other members of the group which were of equal relevance and importance. My findings thus did not support the claims of Grace and Graham (1952) regarding specificity in attitude for different psychosomatic disorders.

Relevance of Stressors as Defined by Selye (1950) *in Psychosomatic Disorders*

So far we have mainly dealt with psychosocial stresses, associated either with the onset of the illness or with the occurrence of attacks during the course of the illness. Such stresses are not necessarily identical in their effects on the organism with the stressors described by Selye (1950) which, by definition, produce manifestations of the General Adaptation Syndrome (G.A.S.). The G.A.S. changes include adrenal stimulation, shrinkage of lymphatic organs, gastro-intestinal ulcers, loss of body weight and alterations in the chemical composition of the body. Some agents are virtually unconditional disease producers because of the intensity of their direct effect on the body, e.g. ionizing rays, great extremes of temperature and severe mechanical injuries. The majority of stressors, however, are conditional, depending on other factors for their manifestations. Among the list of stressors given by Selye (1950) are allergic reactions, infections, intense muscular exercise and marked emotional tension. All these, Selye states, produce the various physiological, biochemical and endocrine changes of the G.A.S. In our asthma series all these factors acted as precipitants of attacks. The immediacy of precipitation of attacks by these stressor agents suggests that they are probably mediated by mechanisms other than those of the G.A.S., which require time for development. With regard to the immediate precipitation of attacks by emotions a neural mediating pathway is probable. There is, in fact, strong evidence that the parasympathetic nervous system is involved (Rees, 1956). There are complex relationships between allergy, infections and emotional tension in the precipitation of attacks of asthma, vasomotor rhinitis and urticaria. Considerable recent work demonstrates a correlation between emotional states and stressful experiences on the one hand with adrenocortical functions on the other. Selye (1957) has shown that the development of manifestations of disease in response to stressor agents is influenced by the type of hormone secreted and by a number of conditions or conditioning factors which influence the effects of these hormones. As Selye (1957) has shown, the adrenal cortex produces anti-inflammatory hormones (such as cortisol and allied compounds) and pro-inflammatory hormones (e.g. aldosterone and desoxycorticosterone). Selye has shown that the same amount of pro-inflammatory hormone, which produces marked kidney damage and hypertension in a rat kept on a high salt diet has no effect on a rat receiving a salt-free diet. The experience of stress in itself can be a conditioning factor, e.g. the amount of cortisone which would markedly inhibit inflammation in a patient who has just undergone a major surgical operation is found to be ineffective in a healthy person. The release of adrenaline, noradrenaline and acetylcholine during the G.A.S. can also influence the effects of hormones. Adrenaline and noradrenaline by their vasoconstricting properties can inhibit the spread of inflammation, whereas acetylcholine by its vasodilating properties can increase the effects of pro-inflammatory hormones. Recently Selye (1958) has shown that cardiac necrosis can be induced experimentally in rats, when exposed to cortical hormones and subjected to immobilization, which he found to be a potent stressful agent. He found potassium and magnesium could prevent these changes taking place. Thus there are many conditions, including hormonal, neurohumoral and biochemical changes in the internal environment, which can influence the development of disease resulting from stress, some facilitating its development and others having a preventive or alleviating effect.

Multiple Causation and Interrelationships of Factors

This brings us to the interrelationships of different ætiological factors in certain psychosomatic disorders. We have noted that plurality of causal factors is the general rule in psychosomatic disorders.

In asthma, vasomotor rhinitis and urticaria, for example, there is clinical and experimental evidence that allergy, infections, physical agents and emotional factors can exert summative effects in producing manifestations of these disorders.

The onset is sometimes due to a combination of stress with allergy or infection. Similarly the response to allergens is influenced by the patient's emotional state and by infections which also are facilitated by certain emotional changes. Emotional states which precipitate attacks of these disorders are mediated by the parasympathetic (cholinergic) pathways. The local tissue changes in vascularity, swelling and glandular secretion due to cholinergic activity have additive effects with some tissue changes produced by allergens and mediated by histamine and infections.

Specificity of response to stress.—So far we find that the stressful stimulus is non-specific for the manifestation of psychosomatic disorders. There is some evidence in favour of specificity of response as shown by the work of Lacey and Van Lehn (1952) who in a longitudinal study of children over many years found a tendency for the same patterns of autonomic response to occur to all forms of stresses and stimuli and that this was relatively consistent when retested over a five-year period.

Although many of our patients tended to react with the same manifestations to various stresses during the period under observation, i.e. six months to three years, there were some who reacted to stress with multiple psychosomatic disorders. There was a group of patients who developed both asthma and peptic ulcer with stress, others asthma, migraine and vasomotor rhinitis. Other diseases associated with asthma were rheumatoid arthritis, ulcerative colitis, neurodermatitis, hypertension, coronary disease, spastic colon, &c. The question of specificity of disease reaction has been recently investigated by Buck and Hobbs (1959). During a five-year period of observation the occurrence of different diseases in the same individual was significantly greater than would be expected if they were unrelated. This is in keeping with the investigation of Hinkle and Wolff (1957) on the illness experience of 3,500 people—U.S.A. residents. It was found that a quarter of the group was responsible for two-thirds of the illness. Clusters of illnesses could be identified in many individuals, the majority of such clusters tending to occur when the individual perceives his life situation to be unsatisfactory, over-demanding, or a threat to security, or with failure to satisfy important personal needs. This applied to all forms of illness, medical, surgical and psychiatric. These findings indicate that the term psychosomatic is applicable to a greater range of diseases than formerly believed.

In conclusion I cannot do better than quote Henry Maudsley who in 1867 wrote: "Life in all its forms, physical and mental, morbid or healthy is a relation. Its phenomena result from the reciprocal action of an individual organism and external forces. Health as the consequence and evidence of a successful adaptation to the conditions of existence implies the preservation, well being and development of the organism, while disease marks a failure in organic adaptation to external conditions and leads therefore to disorder, decay and death."

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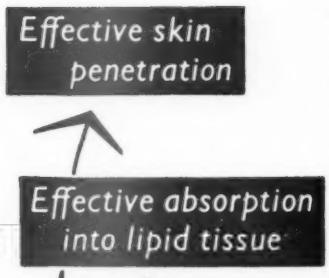

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* Halpern, et al (1948)
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November 21, 1958

Social Factors in the Outcome of Mental Illness

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IN the history of epidemiology there are a number of studies which display the march of logic to a triumphant conclusion—namely, the identification, in the most economical terms, of factors responsible for the inception and subsequent course of a given disease, such as cholera, typhus, or beri-beri. Sometimes, as in pellagra, psychiatry has been the residual legatee of this fundamental work; but, hitherto, epidemiological research in psychiatry has been concerned principally with studies of hereditary factors. Unfortunately, with rare exceptions such as Huntington's chorea, clear-cut genetic information has not emerged: even of schizophrenia it can only be said that there is a definite hereditary factor about whose mode of transmission geneticists disagree.

It is still true that no well-established ætiological theories exist which could account for the major functional psychoses—schizophrenia, affective psychosis and the psychoses associated with senility. This presents a challenge to epidemiological inquiry; but as soon as one tries to take up the challenge, certain peculiarities of mental disorders have to be taken into account. Some of these peculiarities, such as gradualness of onset, prolonged and fluctuating course and the consequences of prolonged interference with social functioning, are found in other chronic incapacitating diseases, but others are not. For example, it is singularly difficult in psychiatry to establish the point at which a patient's symptoms cease to represent individual eccentricity and indicate mental illness. The attitudes of a patient's relatives and neighbours contribute to the recognition of his illness; but it is possible that they may also contribute to its genesis. Environmental influences are believed by many psychiatrists to play an important part in the onset of mental illness; but as yet it has not been possible to establish *which* influences are most important. The two major obstacles are (1) the multiplicity of possibly relevant factors in each patient's social environment, and (2) the relative infrequency of occurrence of psychosis, if first attacks only are considered.

As so often in epidemiology, there are two complementary methods of attacking the problem: the extensive method, which involves studying large populations, noticing sub-groups in which the incidence of psychoses appears to differ significantly from the rest, and seeking other characteristics which are consistently associated with these different rates. We have been indebted to the Registrar-General's office—perhaps especially to Miss Brooke—for many informative and suggestive tabulations on these lines. The other type of inquiry consists in a more detailed scrutiny of a small sample of cases, in order to test the validity of ætiological relationships suggested by extensive surveys or by clinical experience.

My colleagues and I have recently carried out a study of the latter type, in which we ascertained the fate of 240 chronic psychotic men during the year following their discharge from mental hospital. The choice of this particular group was determined by our research unit's interest in the rehabilitation of chronic psychotic patients but we believed that the findings might have wider relevance, if one assumed that social factors associated with relapse in this vulnerable group could also contribute to the onset of psychoses in general.

The major findings of this study, which have already been reported (Brown *et al.*, 1958), were that in addition to the patient's clinical state at the time of discharge two other factors were of great importance for his subsequent progress: his success in finding employment, and the type of household to which he went on leaving hospital. Somewhat to our surprise, we found that the outcome was *worst* for those patients who went to their parents' home,

progressively better for those who lived with their wives or with other kin, and best for those who rented a room from a landlady. This difference in outcome remained within the group of patients who were rated as "relieved" on discharge.

In the course of this investigation, a very detailed interview schedule of information concerning their post-hospital history was completed for 229 out of the 240 patients. Many of the 162 items included in this schedule did not prove to be significantly related to the outcome, but some of these proved illuminating when we re-examined the cases which did not conform to the general trend. For example, we were not able to show an association between household income and patients' success rates; but on re-analysis we found that success was rendered more likely if *either* the patient or the woman of the house went out to work. This was especially the case with chronic schizophrenic patients.

In theoretical discussions of environmental influences which are alleged to contribute to schizophrenic breakdown, two concepts have received especial emphasis: that of the "schizophrenogenic mother", and that of the harmful consequences of "social isolation". In our sample, there was a small group of mothers of schizophrenics who showed extremes of oversolicitude or of domination towards their sons, but this was not always associated with early relapse; an important complementary factor appeared to be the patient's reaction to this type of mothering. Moreover, we were in many cases unable to determine whether the mother's attitude had preceded the first onset of the patient's illness or had developed in response to it. With regard to the "isolation" hypothesis, our data seem to support the view that a certain measure of "social distance", or disengagement from intimate personal ties, is salutary for schizophrenics living in the community: a view which has already been supported by the ecological studies of Hare (1956) and of Gerard and Houston (1953). These are, however, still somewhat tenuous conclusions which will need to be reinforced by confirmatory studies before they can be made the basis for practical recommendations.

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A Longitudinal Study of Patients First Admitted to Mental Hospitals

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ANNUAL statistics of hospital admissions and discharges have many uses, one of which is to consider patterns of release and readmission. For this purpose, however, their value is limited, because patients admitted early in the year have a longer survey period than those admitted later. To ensure that each patient is surveyed for the same length of time, the cards sent from designated mental hospitals to the General Register Office for statutory patients first admitted during 1954–56 have been arranged in an alphabetical index. Leaver or admission cards which indicate a first admission in 1954–56 are paired with first admission cards already in the index and the data they contain are transferred to the index card. Even if a discharged patient enters a designated hospital other than the one in which he was first treated, the data for his two visits will be brought together. The index cards therefore contain a continuous record of periods of hospitalization, referred to here as hospital visits.

Since it is generally accepted that the two years following first admission are of particular prognostic significance in mental illness, this period was chosen for the first follow-up study. A further analysis will be made at the end of five years from the date of first admission and again at ten years. The continuity of the study is being secured by obtaining data for patients entering and leaving accommodation which has been de-designated since the inception of the project. The method of follow-up is to take the patient's first admission date and consider his position on the corresponding date two years later, whether in or out of hospital. For 1954, therefore, it was necessary to wait until all cards for December 1956 had been sent in before the records could be completed. This paper presents

some of the results obtained from data for 1954 admissions.

The following definitions should be noted. "Ever-married" refers to patients who have been married at some time, but whose status on admission may be married, separated, widowed or divorced. Voluntary patients leaving hospital are classified as departures. Temporary and certified patients discharged from the Order under which they were received into hospital and returning to the community are classified as discharges.

TABLE I.—FIRST ADMISSIONS TO DESIGNATED HOSPITALS, 1954. RATES PER 100,000 OF 1951 CENSUS POPULATION BY SEX, AGE AND MARITAL STATUS

		Age groups										
		0–	15–	20–	25–	35–	45–	55–	65–	75–	85 and over	All ages 15 and over
Males:	Single	3	49	99	242	248	246	258	267	308	276	148
	Ever-married ..	—	104	44	77	76	94	124	148	254	392	104
Females:	Single	2	48	92	191	176	214	199	234	346	536	143
	Ever-married ..	—	79	80	123	112	131	137	179	299	383	140

There were 44,047 first admissions; the numbers of single males and females were roughly equal (6,416 and 6,465) but of those who had ever married there were 50% more females than males (18,925 and 12,241). Table I shows that first admission rates for single persons in general exceeded those for the ever-married; at all ages 15 and over the excess was significant for males (difference 44; 2 S.E. 4·17). Single males had higher rates than single females, except at ages 75 and over. The rates for ever-married females exceeded those for males at ages 25–84, and the excess at all ages 15 and over was significant (difference 36; 2 S.E. 2·76).

years are significant as between single and ever-married males (difference 8; 2 S.E. 0·97) and single and ever-married females (difference 7; 2 S.E. 1·0). They are also significant as between single males and females (difference 2; 2 S.E. 1·3) and ever-married males and females (difference 3; 2 S.E. 0·60). The differences between the single and ever-married are partly accounted for by the higher proportion of deaths among the latter, 14 and 11% of males and females dying in the first year, compared with 4 and 7% among single persons. The death-rates in their turn may be linked with the older age-structure of the ever-married groups; this will become clearer when the results for different age groups are compared. It is, however, satisfactory to know that in the four sex-status groups shown, the percentages who were discharged or who departed in the first year were 78, 75, 70 and 75 respectively.

Schizophrenic patients showed a different pattern. They comprised 38 and 26% of single males and females admitted, and 9 and 10% of those ever-married. There were very few deaths in hospital in this diagnostic group; 103 out of 7,020 or 1·5% of the total admissions died in

TABLE II.—FIRST HOSPITALIZATION. PERCENTAGE OF PATIENTS STILL ALIVE AND IN HOSPITAL AT SUCCESSIVE PERIODS OF THE FIRST TWO YEARS

		Percentage at end of				
		1st 3 months	2nd 3 months	3rd 3 months	1st year	2nd year
(*a*) All diagnoses						
Males:	Single	48	28	21	18	14
	Ever-married ..	29	16	12	10	6
Females:	Single	52	33	26	22	16
	Ever-married ..	35	21	16	14	9
(*b*) Schizophrenia						
Males:	Single	65	36	27	23	18
	Ever-married ..	48	26	19	16	12
Females:	Single	68	41	30	26	20
	Ever-married ..	52	28	21	17	12
(*c*) Manic-depressive reaction						
Males:	Single	36	20	15	13	9
	Ever-married ..	21	10	7	5	3
Females:	Single	38	20	16	13	9
	Ever-married ..	23	11	7	6	4

Table II shows the percentages of patients still alive and still in hospital at the end of each three months of the first year and at the end of the second year. For all diagnoses the differences in survivorship in hospital at the end of two the two years under review. They were, however, a comparatively young group, 67% of the males and 52% of the females being in the age group 15–34. Single persons, whether male or female, departed or were discharged at a slower rate

than the ever-married, and the proportions remaining in hospital throughout the two years were significantly higher (males, difference 6; 2 S.E. 2·5; females, difference 8; 2 S.E. 2·5).

Patients with manic-depressive reaction showed relatively rapid rates of departure and discharge: more than 60% of single and over 75% of the ever-married left during the first three months. Here again the ever-married left hospital earlier than did single persons, and the proportions of single persons who remained in hospital continuously for two years were significantly higher than those of the ever-married (males, difference 6; 2 S.E. 1·8; females, difference 5; 2 S.E. 1·6).

Whenever the desirability of making the procedure for admission and discharge less formal is discussed, the question usually asked is whether people would spend the same proportion of time in hospital but pay a large number of short visits instead of one or two longer ones. Two measures can help to answer this; firstly, the percentage of patients discharged or departing who are subsequently readmitted, and secondly, the total proportion of time spent in hospital, irrespective of the number of visits. These measures have been calculated for 1954 first admissions and can later be compared with those for other years.

TABLE III.—RELAPSE RATES; PERCENTAGE OF PATIENTS DISCHARGED OR DEPARTED FROM FIRST VISIT WHO WERE READMITTED WITHIN TWO YEARS FROM DATE OF FIRST ADMISSION

Age groups	Males		Females	
	Single	Ever-married	Single	Ever-married
(*a*) All diagnoses				
All ages	29	24	28	26
Under 15	27	–	32	–
15–	29	14	26	18
25–	31	23	27	23
35–	26	24	28	24
45–	24	23	29	27
55–	28	25	28	29
65–	27	27	31	32
75 and over.. ..	12	33	27	26
(*b*) Schizophrenia				
All ages	34	34	31	31
15–	34	25	30	28
25–	37	35	31	28
35–44	28	37	32	33
(*c*) Manic-depressive reaction				
All ages	26	25	28	26
35–	27	25	29	32
45–	22	23	30	27
55–	34	26	29	30
65 and over	26	29	33	34

Table III shows the percentage of patients admitted for a second visit to hospital among those who departed or were discharged from their first visit. Three sources of error may be involved. The numerator may be understated because some patients for their second visit have entered non-designated hospitals. The denominator may be overstated because some ex-patients have left the country. The numbers involved seem unlikely to be high. Finally, no correction has been made to the denominator to allow for patients who have died out of hospital following discharge or departure. When the differential death-rates are known, a correction factor can be applied; the existing error is more likely to affect the relapse rates in the higher age groups.

Table III shows that, taking all relapsed patients together, both single males and females had significantly higher rates than the corresponding ever-married groups (males, difference 5; 2 S.E. 1·5; females, difference 2; 2 S.E. 1·5). The rate for ever-married females was significantly in excess of that for the males (difference 2; 2 S.E. 1·4). For schizophrenics there was little difference between the relapse rates at all ages for males and females and no difference between the rates for the single and ever-married of each sex. The rates were high among single males aged 15–34 and ever-married males aged 25–44. In the older age groups the numbers were too small for any significance to be attached to the rates. Among manic-depressives a relapse appeared rather more frequently in the older than in the younger age groups, but the rates for all ages for the four sex-status groups varied little from one another and their differences were not significant.

Of the 44,000 patients first admitted in 1954, only 2,360, or 5%, returned for a third visit to hospital. It will be possible later to compare the proportions of higher order admissions in 1956 with those for 1954 and see whether there has been a tendency towards more frequent admissions and discharges.

A study of this kind tends to concentrate on patients who return again and again to hospital. A more hopeful aspect to consider is, that of the 44,000 admitted, 34,000 were discharged or departed from their first visit and of these 25,200 did not return for a second visit within two years from the date of their first admission. If the crude death-rate of 11·3 per thousand in 1954 were applied to the latter number, even for the whole two years, only about 600 deaths might be expected, reducing it to 24,600. This would mean that 72% of those who were discharged or departed from their first visit could be expected to complete the two years from date of first admission without returning to hospital.

TABLE IV.—TOTAL PERCENTAGE OF TIME SPENT IN HOSPITAL, IRRESPECTIVE OF THE NUMBER OF VISITS, IN THE TWO YEARS FOLLOWING FIRST ADMISSION

	Percentage of two years											
	–5	–10	–15	–20	–25	–30	–40	–50	–60	–70	–85	–100
(*a*) All diagnoses												
Males: Single												
15–24	23	14	11	10	8	5	6	4	3	3	3	10
25–44	22	14	10	9	5	4	6	4	3	3	3	17
45–54	23	15	11	8	4	3	3	3	2	2	3	23
Females: Single												
15–24	24	14	12	10	7	5	6	4	3	2	3	10
25–44	21	16	11	9	5	5	6	4	3	2	3	15
45–54	19	18	9	7	6	3	5	3	4	2	4	20
Males: Ever-married												
20–34	43	19	11	7	5	3	3	2	1	1	2	3
35–54	38	23	11	7	4	3	3	2	1	1	1	6
Females: Ever-married												
20–34	38	22	13	7	5	3	4	2	1	1	1	3
35–54	35	22	12	7	4	3	4	2	2	1	2	6
(*b*) Schizophrenia												
Single												
M. 15 and over	10	9	11	11	7	6	7	5	4	3	4	23
F. " " "	9	9	11	10	8	6	8	5	3	3	3	25
Ever-married												
M. 20 and over	18	13	13	9	8	5	5	3	3	3	4	16
F. " " "	15	15	13	9	7	5	7	4	3	3	3	16
(*c*) Manic-depressive reaction												
Single												
M. 20 and over	28	19	11	8	5	3	4	3	2	2	2	13
F. " " "	23	20	11	9	5	3	5	4	3	1	3	13
Ever-married												
M. 25 and over	36	24	12	7	4	2	3	2	2	1	2	5
F. " " "	33	24	13	6	4	3	4	3	2	1	2	5

Table IV shows the total percentage of time spent in hospital irrespective of the number of visits paid. The percentage distribution of total time was calculated for each five-year age group and age groups with similar distributions were combined. Among single male schizophrenics, for example, 10% spent up to 5% of the two years in hospital, i.e. about five weeks, and 9% spent over 5 and up to 10%, i.e. rather more than ten weeks. The distributions suggest that there were two principal types of patient involved—a large percentage who spent a total of less than six months in hospital and a second group who spent the whole time there. Of the 23% of single males who spent 85–100% of the time in hospital, 18% were there for the whole two years. Table IV shows the similarity of the time distributions for single persons and those for the ever-married. The latter included a higher proportion of persons with short total time in hospital than did the single groups, and a smaller proportion spending from 85–100% there. The distributions are, in fact, more favourable to the ever-married than to single patients.

The majority of manic-depressives spent not more than 15% of the total time in hospital, i.e. fifteen to sixteen weeks. Again, the advantage is with the ever-married groups, of whom a larger proportion than among single people spent only a short proportion of time in hospital and therefore longer outside.

The results for all diagnoses show patterns which do not differ greatly from those shown by the schizophrenics and manic-depressives, and this would rather be expected, since these groups between them comprise 42% of the total admissions. It can be seen that with increasing age, the percentage of patients spending a small proportion of the total time in hospital decreased, whereas the proportion spending 85–100% increased. This was found to be true for schizophrenics and manic-depressives also.

An analysis linking, for relapsing patients, the duration of first visit with the time out of hospital before readmission showed that the mean periods before relapse seemed to be slightly longer for females than males, but that there was little variation between single and ever-married persons. There was some evidence that, except for ever-married females with manic-depressive psychosis, longer first visits were associated with longer average time before readmission. This applied only to first visits not exceeding six months; for longer durations the frequencies were too small to make the means worth calculating.

From the longitudinal study of admissions, discharges and readmissions, some patterns of release and retention appear to be emerging. Comparison with the data for 1955 and 1956 may make it possible to verify these trends.

Meeting
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The Growth of an Organization for Preventive Medicine

PRESIDENT'S ADDRESS

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I HAVE chosen this subject, which fundamentally consists of reflections about the Medical Branch of the Royal Air Force, not only for the obvious reason that I was privileged to be a member of the Royal Air Force for a long time, but also because that Branch seems to me to provide, as does any similar Service organization, a pattern in miniature of preventive medicine referable to any population or environment or occupation. Again, because of the comparatively recent emergence of the Royal Air Force as an entity, it is possible to start consideration of its Medical Branch from a point within present professional memory. I should, I think, place this point for the purpose of this Address as the year 1920, the year for which the first Annual Report on the Health of the Royal Air Force was compiled, although the Branch was in being somewhat earlier.

This definition of time is not the only definition which has caused hesitation, because I have been in some doubt about the term "Preventive Medicine" itself. Seen in a Service setting, almost every activity of a Branch concerned with health or sickness has some preventive aspect. But I remain unrepentant for using the term when I consider that doubts about the limits of this field have been evident in the wider world of medicine. For example, sciences which I once knew as Sanitation or Hygiene, or perhaps Public Health, have in many places been re-defined, or at any rate re-named. To me all this is merely evidence that medicine is in the end a unity: that curative medicine apparently concerned with the individual must reach out to the community in preventing illness, and that preventive medicine must search back to the individual.

The period which I have chosen to survey is that for which published records are available, from 1920 until the end of the Second World War. Annual Health Reports carry references up to the beginning of 1938, and the volumes of the Medical History of the Second World War dealing with the Royal Air Force Medical Services are available to complete the picture.

Organization.—The medical element of a Service must be conditioned by the aims of the parent Service, and it goes without saying that maintenance of the health of air crew has always occupied a prominent place in the responsibility of the Medical Branch of the Royal Air Force. But preventive medicine must take account of more than occupations—and certainly more than one occupation—however important, and general problems of nutrition, environment, climate, clothing, prevalent diseases and so forth are familiar to medical officers of any service. Again, doctors must be disposed according to the numerical and geographical distribution of the population which they serve. In the case of which I speak the population was scattered over many parts of the world, and seldom in large numbers in any one place. The medical organization for prevention of ill-health was therefore served largely by those doctors who were at the same time charged with the treatment of individual cases of illness.

The size of the active R.A.F. population varied from 30,000 in 1920 to 60,000 in 1937. A rapid increase occurred during the war years, and the wartime population of the Service (including the Women's Service) reached a peak of over 1,000,000. An index of the size of the total supporting medical organization may conveniently be given by means of the ratio of medical officers per thousand of total population. For the smaller pre-war population, this ratio varied between 4 and 6. As the population rose, the ratio fell, and at peak population was 2·15. It is not possible to say how many of the doctors were at various times engaged directly in preventive medicine. Supervision and advice in this field were among the chief tasks of medical officers on headquarters staffs of Commands and Groups, a small percentage of the whole. But medical officers of individual units formed at any one time the majority of doctors, and carried out much of the field work of prevention.

In addition to medical officers, the Medical Branch had at disposal its nursing service, and an establishment of medical auxiliaries. Members of the nursing service were almost entirely employed in hospitals. In peace there were not many medical auxiliaries who might correspond fully with the Public Health Inspector of civil life, and the wide scatter of small units demanded that nursing orderlies employed on general

medical duties should have knowledge of hygiene and sanitation as well as of the nursing of the sick. It is a pleasure to record that a high degree of interest in the field of prevention, and a high degree of competence was widespread among them. But it will be appreciated that a very considerable burden of responsibility for maintenance of health was inevitably carried by individual medical officers.

The population.—While a Service has problems of preventive medicine similar to those of civil life, it begins with some advantages. For example it can within the limits of supply and demand select its population. Thus almost until the outbreak of the War the active population served was very largely young adult male. A survey of recruiting records for airmen is of some interest in its reflection of the quality of recruits.

The first Health Report, that for 1920, analyses the records of accepted recruits by average physical measurements classified by age, by previous occupation, and by region of origin. There was little variation in average height and weight between men with recorded occupations before entry, and little difference in these qualities when related to geographical origin; the Scottish recruit was, however, six months older than the average age of recruit, was shorter than average by 1¼ in. and was heavier than average by 1 lb. The average age of all accepted recruits was 20½ years, height 5 ft. 6 in. and weight 9 st. 2 lb. These figures may be compared with the average figures for cadets accepted in that year for flying duties; age 18½ years, height 5 ft. 9 in., weight 9 st. 10 lb. The principal single cause of rejection of airmen recruits was, in the years of peace, recorded as dental defect; however, quite early, in 1923, it was realized that the contribution which a man might make could outweigh physical defect, and in that year skilled tradesmen were acceptable if their dental deficiencies were corrected by dentures. This solution is not as easy as it sounds. In certain places abroad, dental assistance was in the past difficult to obtain, and in one area at least a journey of upwards of 100 miles was involved, so that dental fitness was important. While the medical officer could at need deal with an emergency involving extraction, he was not able to carry out any but the simplest conservative treatment and he certainly could not repair broken dentures. The principal single cause of rejection of applicants for flying duties was a visual standard below that demanded. In another field, a record in the Report for 1934 states that of over 2,000 recruits accepted, 32% had not been vaccinated.

Nutrition.—Again a Service can arrange, within limits, the nutrition of its members, at any rate avoiding undernutrition from the point of view of quantity of food supplied. It may not, however, be a simple matter to ensure everywhere that balance in diet is maintained or that accessory food factors are present in sufficient amount. The latter consideration was, no doubt, the reason for the provision at one period of wheat-germ in the ration for certain areas overseas, but in retrospect, it appears that more might have been learned from this episode than was, in fact, the case because there is no record of scientific follow-up. However this was thirty years ago, and no clinical manifestation of avitaminosis B was recorded.

A more precise investigation was made in 1937 in relation to the vitamin C reserve of airmen on a station in this country. The test population consisted of 50 airmen; urinary ascorbic acid excretion was estimated, and observation was made in response to test doses. The average excretion was 15·5 mg. per day, the range being 24·4 to 8·45 mg.; the last figure was given by a man who was married and lived away from the station. The response to three test doses of 700 mg. of ascorbic acid showed a state which was regarded as unsatisfactory. 2 men responded to the first dose, 18 to the second, 22 to the third and 5 did not respond; thus 22 of the total were regarded as possessing a minor degree of deficiency of vitamin C and 5 a more marked degree. In 3 cases the full number of test doses was not given and no record is made for them. 5 individuals in a mess where orange juice was provided at breakfast and which probably gave in general a more varied diet were also examined. Among them the average daily excretion was 30·5 mg., the range being from 55 to 23 mg., and all gave a massive response to the first test dose of ascorbic acid.

Water supplies.—The gradual improvement in provision and control of water supplies may be traced throughout these Annual Health Reports, and by 1937 the position on established stations was satisfactory. Samples were examined chemically and bacteriologically at least once a year in all cases, whether supply was derived from established water undertakings, or whether it was provided by the Service. In analyses of doubtful result investigation of the supply was undertaken. It may seem superfluous to have examined samples from public supplies, but many stations were large in area, the internal piping was extensive and local storage by water tower was necessary where large quantities had to be used from time to time; examination in these cases gave some evidence of integrity of

tanks and piping. In relation to water provision in the field an attempt was made to mechanize provision of small supplies. A water sterilizing unit, operated by a 4 h.p. petrol engine, was developed in the late 1930's: this delivered 500 gallons of purified water an hour; filtration was through a kieselguhr filter, and chloramination dosage which was automatic could be regulated as necessary for the raw supply. Chloramination was achieved by interaction of ammonium chloride and sodium hypochlorite formed by electrolysis of salt solution.

Diseases.—Statistical records of diseases, disabilities and injuries occupy the prominent place in the Health Reports as would be expected. The diseases associated traditionally with forces operating overseas as well as at home all have their place, except that typhus fever presented no significant hazard. But it is surprising to note in the first report of all (1920) the preoccupation with sandfly fever as a cause of disability. A chart of incidence showing in one area abroad the incidence in each of the months of May and June to be approximately 250 per thousand of strength goes far to explain the concern with the disease. Again, in the report for 1922, it is recorded that sandfly fever accounted for more than one-quarter of the total cases of significant sickness overseas.

This experience led to action of various kinds. In the Report for 1921 a communication is recorded from a medical officer advocating a heroic form of treatment in order to reduce time lost through the illness. In the same report an extensive research is described to investigate a finding which suggested that a spirochæte was the causal parasite; it was concluded (it seemed rather regretfully) that no claim could be made for the specificity of the spirochæte isolated.

The Report for 1922 contains a record of work which is in my view classical. An investigation was begun by the Royal Air Force Sandfly Fever Commission in Malta in the summer of 1921. The habits of sandflies were re-studied, the flies were successfully reared in captivity, and their life history elucidated. The limits of atmospheric temperature, atmospheric humidity, earth temperatures and wind force compatible with a life cycle of seven to eight weeks were defined. Transmission of the virus of phlebotomus fever from generation to generation of flies was discussed, and, most important from the point of view of the Service, detailed recommendations on prevention were made, ranging from treatment of breeding grounds to the scale of electric fans needed in barrack rooms of different sizes to discourage the attention of sandflies. It might be possible to raise an eyebrow occasionally, for example at the final suggestion of all—that men of older residence who also had previously suffered from sandfly fever should occupy the corner beds in barrack rooms (likely to be more open to sandfly attack) leaving the less infested middle of the room to the newcomers. Elsewhere in the same Health Report there is a table giving frequency of attacks of certain diseases and showing that 176 out of 1,600 individuals suffered more than one attack of sandfly fever. But this comment is a quibble after the event, and the common sense of the suggestion made at the time is I think undeniable. In any case, tracing the course of sandfly fever in the overseas areas chiefly affected, it is of interest to note that after 1923 a considerable drop in incidence was recorded.

All the Health Reports contain, as one might expect, detailed analyses of the incidence of dysentery and of malaria, and it is interesting to note that with the passage of years the mastery over dysentery was more evident than over malaria. This could be predicted in a Service setting, considering the ætiology of these diseases. But the observation gives opportunity for a comment on the practice of preventive medicine which goes beyond a Service environment. Speaking broadly, a great deal can be done by the preventive organization itself to control dysentery. Water can be treated, fly breeding grounds can be searched out and eliminated, food supplies can be made reasonably safe, carriers of disease can be detected and their immediate influence extinguished. All these can be done without demanding any particular effort from members of the population at risk. But the situation regarding malaria in the years up to 1937 was considerably different. The time was not then in sight in many areas abroad when the mosquito could be effectively banished. It could certainly be pushed farther and farther away from living centres by drainage schemes but seldom far enough. So personal precautions were demanded. Buildings could be provided with mosquito gauze, mosquito nets could be provided for sleeping. Individuals could be advised to clothe themselves appropriately during the evening and night. But unless those who directed preventive measures could induce the population at risk to act, they could not expect great success from their efforts. Gauze doors could be propped open for coolness at night. Mosquito nets might be in disrepair, or not let down early enough, or simply not used. Advice on clothing, if interfering with comfort, might well be ignored. All self-evident, no doubt, and I suppose banal, but bearing the lesson that the practitioner of preventive medicine must, in addition to his professional ability, possess or

develop a very considerable ability as a salesman, persuasive enough to induce his customers to pay in the coin of forethought, or inconvenience or even discomfort for the intangible of health, remembering that the average healthy person is inclined to think "It couldn't happen to me".

There were of course other anxieties than these in overseas areas: for example, as reported in 1932, the discovery of a considerable nidus of schistosomiasis in an area where it had not previously been reported, or in 1937 the protection against yellow fever of the members of a cruise by air to West Africa, and also the measures needed on this flight to avoid transference of mosquitoes. Details of this episode are of interest in relation to later experience in this area during the Second World War. In all, 54 men were involved—35 crew members and 19 men held in reserve. As a protection against yellow fever these men were inoculated with serum and virus, as was then the practice. There was little or no immediate reaction, but three to four months later 7 of them developed jaundice. Pressure-spraying of each aircraft with insecticide was carried out twice daily, and also just before leaving any stopping place. Malaria was also a hazard and a dose of 5 grains of quinine was taken by each man daily, and mosquito nets were used. There was no illness on the cruise referable to the undertaking, but 4 men out of the 35 at risk developed primary malignant tertian malaria within fourteen days of the end of the cruise.

Still on the subject of disease and disability, and turning to the force at home, we find that influenza, nasopharyngitis and tonsillitis were prominent among illnesses causing significant loss of time. It is to be noted in the Reports that, even at periods when nasopharyngitis and tonsillitis showed high incidences, the figures of illness attributed to the common cold remained low. Looking back to this period the reason for this anomaly is fairly clear, and I must plead equally guilty with others in what I now feel to have been a misuse of terms in many instances. As I remember the situation, my feeling was that the term "common cold" was imprecise, and unsuitable for a patient in hospital, not reflecting that the term nasopharyngitis was, if anything, still less precise.

Influenza understandably drew considerable attention from the point of view of prevention. In routine preventive measures, it took its place among other droplet infections, but specific measures were considered. A description of an investigation in 1928 begins, rather sourly I feel, with the following words: "An attempt was made to estimate the prophylactic value of so-called anti-influenza vaccine". This was indeed a considerable investigation, comprising 969 inoculated subjects and 1,041 controls. All were between the ages of 15–18 and all lived in comparable style on the same station. Two vaccines from different sources were employed. The conclusion drawn was that no claim could be made that anti-influenza vaccine lessened the incidence of influenza or of acute nasopharyngitis in any appreciable degree. It was remarked also that the results obtained with the two vaccines employed were almost identical. Considering the amount of work involved in this trial, carried out I think mainly by one worker, the disillusioned tone of the report can readily be understood.

Among the list of conditions affecting the well-being of a population of adolescent and young adult males may be mentioned those of nuisance value—not often significant from the point of view of risk to health, but nevertheless time-wasters: impetigo, scabies and pediculosis. The last of these was, at home, of least importance demanding mainly diagnosis, because in a male population treatment was not difficult, and prevention was a matter of routine cleanliness. Prevention of the two other conditions remained a considerable problem. Impetigo appeared to attack clean and dirty alike. In relation to scabies we now know that much effort given to prevention might have been saved if a solid attempt had been made at an early stage to define the epidemiology of the condition.

Environment.—Housing, heating, lighting, clothing and effects of climate all received considerable attention in the Annual Reports. Here, as in many fields, change may not always be rapid, and not until 1936 was it noted that the open-neck tunic replaced the former type with the stiff upright collar, and that lightweight cotton and wool mixture shirts and pyjamas replaced the heavy traditional flannel garments.

These pre-war records covered, although they did not fully report, a period of change of outlook on the effects of tropical climate. Until approximately 1925 the spine pad was compulsory wear in certain tropical areas, and the topee remained so in all tropical areas until early in the war. But from 1930 onwards there was a growing body of opinion which questioned existing views on the ætiology of heat effects, and in particular the views on the effects of the rays of the sun. A number of medical officers in one area satisfied themselves by personal experiment that, once acclimatized, they could safely expose themselves in a state of nature to the midday sun in the tropics, and they were not all Englishmen, although some may on other grounds have been considered mad dogs. When experiences of this kind were weighed during the

war, and considered together with more academic researches on heat effects, there was little risk in breaking with the past and advocating more comfortable tropical clothing, based on physiological rather than on mystical principles.

Occupations.—The first Annual Health Report differentiated nine different trade groups in the Royal Air Force, although in the eyes of the present day there were some strange bedfellows in certain groups. For example, listed under the general heading of "metal workers", were blacksmiths, stokers and dental mechanics. Nevertheless, for practical purposes the groups were adequate, and a table gave the experiences of each group in relation to significant diseases.

Because of the industrial character of many of its tasks, occupation in the Royal Air Force has always demanded close attention to preventive measures and it is fair to say that risk of disability due to occupation has received its due amount of consideration. This may be exemplified by the section in the Report of 1937 which sets out an investigation in conjunction with H.M. Medical Inspector of Factories into the conditions of workers under R.A.F. control using mesothorium, a radio-active compound employed in painting luminous dials. The rules for storage and handling of the material formulated for the Service in that year as a result of the investigation bear considerable resemblance to those embodied in the Factories (Luminising) Special Regulations, 1947.

But the occupation of greatest importance to the Service is the flying of aircraft. From the earliest days this has received the close attention of all elements of the Medical Branch, and it is indeed difficult to decide in this regard where prevention ends and therapy begins.

On its formation the Royal Air Force inherited the very considerable foundation of aviation medicine gained from distinguished workers who had studied the problems in the Royal Flying Corps and the Royal Naval Air Service. In particular they received the basis of a scheme of selection for flying duties which still influences this aspect of preventive medicine, although study and advancing knowledge have modified the original concepts. These processes of selection for employment are aspects of preventive medicine; they are designed to the end that individuals will not suffer from their employment through unsuitability and that they will not be dangerous to themselves or to others. There is clearly no difference in principle between the elaborate selection for pilot duties and, say, the test of colour vision carried out on those who must differentiate red and green in an industrial setting.

In technique of selection of flying personnel growth appears to have followed a pattern familiar in other emerging aspects of medicine—the search for principles, intricacy resulting from following principles not yet clarified by experience, undue emphasis from time to time on one or other feature, and gradual simplification, as time and research indicate more clearly what is the seed and what is the husk. Considering the circumstances in which the examination for fitness for flying was elaborated, I have always thought that the examination procedures were well conceived. Those who first took to flying—and there were few until after the first decade of this century—may be said to have selected themselves. In general they were those with a scientific or technical interest in aerodynamics or engines, and those who saw in aviation a sport, spiced with danger, and demanding similar qualities to steeplechasing or driving racing cars. When the need for pilots grew in the First World War it became apparent that a general physical examination and the usual tests for visual acuity were insufficient. After close study, physiological tests were evolved designed to forecast performance in conditions of diminished oxygen tension, quickly-changing atmospheric pressures and change of orientation in three dimensions, demanding, as far as could be seen, qualities of stamina and stability in the heart-lung system, ocular balance as well as visual acuity, otological integrity, and good neuromuscular control. Standardization was the aim, and methods of application of the tests were devised to allow records to be made, where possible, in numerical terms. After experience the stringent requirements of certain tests were questioned, or indeed the need for certain tests, but until the 1930s only minor changes had been made in the procedure based on First War experience.

I have dealt with this topic of selection at some length not only because of its prime purpose of selecting air crew, but also because the records so made for all these men formed a considerable part of the basis of preventive medicine applied during their later careers in flying. In the field of prevention referable to this occupation, the practitioner was again the same medical officer responsible for treatment. One of his duties was the periodic examination of air crew, and he had been trained, and wherever he was stationed possessed the apparatus, to carry out special tests comparable with those of the initial examinations. He also had records of all previous examinations. Comparison of serial records was intended to, and I think did, give an indication that all was likely to be well, or that some deterioration demanded investigation.

It had early been appreciated that the psychological aspects of flying were of great importance but in this area it was not possible to reduce records of performance to numerical terms. In the days of small compact flying units, the medical officer lived with the squadrons, and knew the flying personnel in their daily lives. He had received some instruction on the manifestations of the neuroses and on anxiety states, and realized that his duty was, as far as possible, to anticipate their occurrence especially by noting changes in the habits or character of his charges. He was encouraged to gain insight into his task by flying as passenger with squadron members, or in some cases by himself learning to fly, a specially modified course for medical officers being arranged. Needless to say, the young doctor on duty for the first time with a flying unit was quite unsure of his surroundings or indeed of his real duty. But interest grew quickly, and in most cases became a scientific interest as well as a personal interest in the men themselves. In my own case, I think that a rhyming jingle which I heard at my first station made me realize, vaguely enough, that there might be an "epidemiology" of errors of performance, as well as an epidemiology in the more usual sense. This rhyme was:

"Skilful pilots never oughter
Boil their radiator water"

and its basis was that forced landings sometimes occurred because pilots omitted to open the shutters which on one type of aircraft ventilated their water-cooled engines. I began optimistically to try to find out if there was a pattern in this defect of performance, but failed because I could not detect any pattern when the universal reason given was "I forgot", because I was not a psychologist and could not proceed from this point, and because people generally do not welcome discussion of occurrences of which they are slightly ashamed. This was in any case a minor and transient problem. The average medical officer quickly became similarly interested; those who were above the average in insight, personality and enthusiasm gathered a body of experience which was to prove of the greatest value in the conditions of the Second World War.

Behind this field work was a small central organization for more formal research into physiological and psychological aspects of flying, and it was probably adequate in the earlier days between the wars when progress in the performance of aircraft was not rapid. But if I may venture an opinion it was ultimately insufficient because the allotted establishment remained too long restricted. However, the risk of such slender effort was appreciated, and before the war the Flying Personnel Research Committee was formed to further research in this field. The late Sir Edward Mellanby became chairman of this committee, and gathered round him civilian scientists eminent in the fields of physiology and of psychology who by their own extensive work as well as by their advice to Service workers made rapid progress possible in the task of ensuring that the man in the aircraft could exploit the rapid increase of aircraft performance.

A link had to be made between the laboratory and the field. Problems in the field had to be recognized, and laboratory results had to be translated into practicable measures. This link was formed in the war chiefly by the organisation of a body of medical officer pilots, who were trained to the standard of operational pilots, in some cases those very medical officers who in pre-war days had shown themselves to be outstanding in the care of the aircrew, and in general their direct descendants in a professional sense.

Research.—Elements of research in various fields have already been mentioned, and inevitably the volume and nature of research into aviation medicine overshadows all else.

But growing experience was evident in smaller ways. The Reports for 1921 and 1922 tabulate the results of a questionnaire designed to assess the value of prophylactic self-disinfection in the prevention of venereal disease. The questionnaire was answered after the event by those who had contracted disease, and appeared to indicate that attack was two to three times as frequent among those who had not properly disinfected themselves as among those who had. No doubt the obvious defects in such an inquiry were realized because such analyses are not recorded in subsequent years. But in 1930 a record is made of the results of prophylactic disinfection carried out by a trained orderly on those who reported to him after exposure. This scheme, I suppose, lent itself to a prospective investigation because at the time a record was made of all attendances; assessment showed that within the period of observation 1·9% of those treated developed disease. This seems an advance in technique of investigation, though leaving unanswered the riddle of the effect of taking no preventive action whatever.

The Second World War.—The rapid increase of the Service during the war has been mentioned, and the consequent dilution, if I may use the word, of the concentration of members of the Regular service by members of the Reserve services.

However, the fundamental organization of the detached station or unit as the operational element remained recognizable, and the necessary adaptation of preventive measures was less difficult than might have been feared. Perhaps I should say that the high quality of the diluent medical officers and medical auxiliaries who manned the Medical Branch probably made the transition appear less difficult.

There were, of course, features which might have been more satisfactory. In the arrangements for accepting recruits, a time schedule was fixed to make intake as rapid as possible. Inoculation and vaccination were among the processes of initial entry, and the schedule was somewhat delayed because insufficient weight had been given to the extent of disability which may follow vaccination; the organization was surprised by the proportion of primary vaccination necessary, although indications had already appeared in earlier Health Reports in relation to peacetime recruitment.

Again ablution accommodation for airwomen was at first a cause of dissatisfaction because, arranged by men, it had not been foreseen that the usual overhead shower is unsuitable for a woman's coiffure, and that women demand greater privacy in their ablutions than men.

In the West African theatre, the initial incidence of malaria suggested that the standard of salesmanship before the event in this area of prevention had not been sufficiently high. On the other hand, the ready acceptance of measures to prevent contraction and transmission of yellow fever was in general notable and gratifying.

Conclusion.—It is now time for me to do what I can, after these rambling reflections, to trace my way back to the subject of this Address, and I shall try as a beginning to define what to me is the meaning of growth in this context.

First, growth is not, I submit, necessarily synonomous with numerical increase in an organization, nor with greater and still greater resources of machines and appliances. Indeed I can imagine circumstances in which, by true growth, an organization for preventive medicine may decrease in these regards. I suggest that growth is a growing up in outlook and approach and experience: to be ready to adopt new ideas, but not to accept them blindly: to be willing to learn from the experience of others but also to lose no chance of adding to knowledge by study and exertion in one's own field: to remember past experience without being hidebound by the past: to be prepared for unusual situations and not to be forced into hurried improvisation.

Measured against these standards may I rashly comment on a few features of the growth of this particular organization. I say "rashly" because it is not easy in all this for me to be sure of objectivity. However I would suggest that there was growth when the organization undertook a comprehensive research into sandfly fever, and did not remain satisfied merely with a promise of reduction in length of disability by a proposed form of case treatment. It failed to grow when it did not try to assess the value of added wheat-germ in the diet, but grew when it estimated the levels of ascorbic acid in another dietetic situation. It failed to grow when at the beginning of the war it forgot past records indicating that much primary vaccination would be needed among recruits. It grew notably when it invoked the assistance of experts outside its own organization in problems of flying, and grew also by the effort made to know its own field by the encouragement of medical officer pilots.

The surrounding of this Address is unashamedly parochial. But it seems to me that extended into the general field of preventive medicine there may be some points of application, even if only the thesis that there is a greater overlap of preventive and curative medicine than is sometimes believed.

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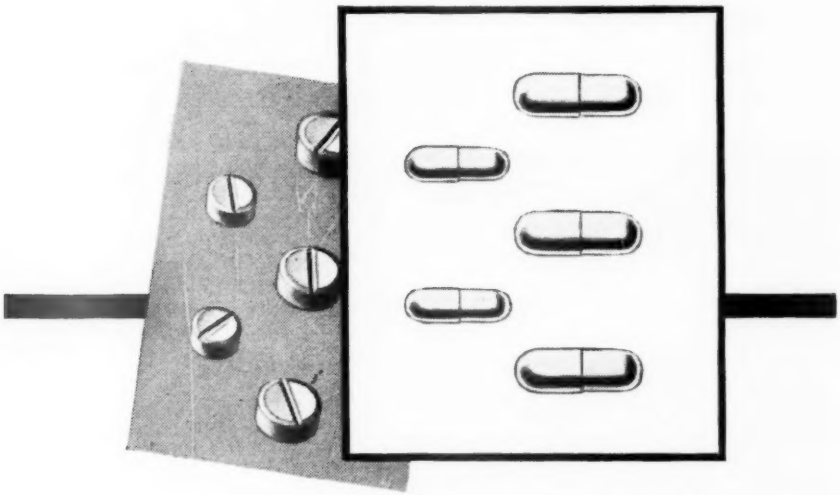

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Meeting
November 4, 1958

Dr. WALTER P. BLOUNT (Milwaukee, U.S.A.) read a paper on **Osteotomies of the Upper End of the Femur.**

Meeting
December 2, 1958

SYMPOSIUM ON THE TREATMENT OF FRACTURES OF THE SHAFTS OF THE LONG BONES

Mr. William Gissane (Birmingham):

Internal Fixation of Fractures

I have been told that my reputation in some quarters is that of an "early internal fixer" of all fractures of the long bones. Yet if my practice were restricted to one or other method of treatment, I should unhesitatingly choose the closed manipulative method for early treatment. Happily I am not so restricted.

I believe there is now a very strong case for early open reduction and rigid metal fixation of the more severe types of both closed and open fractures of long bones—those that cannot be reduced to a relatively stable position and maintained in good alignment by closed methods, but in which these desirable conditions can be obtained by open reduction and metal fixation. Further, I believe that the more anatomical the reduction and the more rigid the internal fixation the earlier is the return of function, the more normal the result and the less frequently will degenerative changes occur in adjacent joints.

The main argument against early open reduction and metal fixation of closed, and open, fractures, has been the supposed high risk of bone infection. This dates back to the days when the metals in common use had a high or a moderate rate of corrosion with resulting irritative and toxic effects on the body tissues. It was early in 1956 that complete standardization by manufacturers was achieved in this country in the manufacture of plates and screws of the safer metals.

Now that the modern metals 18/8/MO and Vitallium are in general use and are known to give no trouble from corrosion in over 90% of cases and minimal effects in the remaining 10%, the evidence is that open reduction and internal fixation do not carry high risks of bone infection. In a series of 45 closed fractures reduced early and held by the safer metals we had three infections, all superficial and none involving bone. In another series of 100 open fractures we had a 12% infection rate in those wounds that were thoroughly cleansed and the skin closed but the fracture not plated; in the control series in which we added internal metal fixation (and these incidentally were more severe types of fracture) our infection rate remained at 12%. None was an obvious infection of bone; all involved the soft tissues only and the majority were minimal.

On this experience we believe that bone is not particularly susceptible to infection. We believe that in the past the early clinical effects of corrosion of metal on adjacent soft tissues, namely, red, shiny, hot, tender and œdematous skin (a condition that can go on to wound breakdown and *then* infection), have been mistaken for primary bone infection.

Since abandoning the corrosible metals this reaction has almost completely ceased and when better metals are eventually discovered will undoubtedly be completely eliminated. I believe that once dead spaces and hæmatomata are eliminated by early gentle surgery, exact reduction and rigid fixation, the hæmostasis and wound closure without tension achieved, the battle against wound infection is largely won. This is not to be taken as an excuse for relaxing any of the aseptic and antiseptic precautions in our theatres. With closed fractures, primary wound infection is due mainly to organisms on the skin and carried into the wound during the operative act. Thorough cleansing of the skin before operating on a painful fracture can be carried out only under general anæsthesia by either the surgeon or

his well-trained assistant; *this is an essential part of the operation in both closed and open fractures.* I would add to these precautions against infection by supplying all theatres with bacteriologically clean air forced in at roof level under pressure with an exit near floor level, giving a complete air change twenty times an hour. There is now unmistakable evidence that this measure limits to a large extent the possibility of added infection during the operation.

The conservative school maintains that the manipulative treatment of closed fractures eliminates all possibilities of infection. This is not so. Many fractures so treated come later to open operation for various reasons—deterioration in position, mal-union, delayed union and non-union. The infection rates resulting from subsequent open surgery should be debited against the conservative method.

By early open reduction I mean reduction within a few hours of the injury; in some fractures this is vital. In others, when a choice can safely be made, I prefer a delay of seven to twenty-one days before open reduction and internal fixation. There is evidence that such delays considerably improve the rate of bone union. Smith (1959) has a series of 52 fractures of both bones of the forearm treated by delayed plating. 50 were soundly united in six months and the remaining 2 within twelve months.

I have become more and more convinced that internal fixation of long bones should be as rigid as possible. Even after an exact reduction of a fracture, a plating that is initially imperfect can become progressively more imperfect as a result of slight movement and this occurs even when external splintage is added to internal fixation. Such movement causes irritation, decalcification and further loosening of the screws and the plate. Against this, a plating that is initially mechanically perfect tends to stay so for very long periods. This is of considerable importance in all fractures that from the nature of the injury must be slow to unite. Of all methods of internal fixation with which I am familiar none has, in my view, the potential virtues of the plate designed by my hospital colleague, Mr. John Hicks. "Potential" because he has not yet designed the plate to fit the many anatomical curves and twists of the shafts of all long bones.

Finally, all fractures are wounds, not only of bone and periosteum but often of many other covering tissues. All displaced tissues should, if possible, be approximated without tension and rested until they unite. A full understanding of the detailed nature of these wounds (and those resulting from high-speed road traffic accidents can be extremely complicated) demands very early clinical as well as full radiological investigations—sometimes repeated clinical examinations before an exact diagnosis is possible and priorities on the urgency and the nature of treatment correctly assessed.

(Mr. Gissane then illustrated with slides the various points he had propounded.)

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Mr. John Charnley (Manchester):

Our understanding of the basic processes which govern fracture repair in long bones is still far from complete. A vast amount of experimental work on rats and rabbits has done little or nothing to help us to decide the best treatment for a fracture of the shaft of the tibia in the human subject. There are still important lessons to be learned from clinical observations made on the behaviour of human long bones during different methods of fracture treatment.

I shall confine myself to three basic features of fracture healing, all of which are controversial, and endeavour to indicate how I think they are related to the practical details of treating a fracture of a long bone such as that of the tibia:

(1) The fallacy of accurate reduction.

(2) The fallacy of defective osteogenesis.

(3) The fallacy of absolute fixation.

The Fallacy of Accurate Reduction

It is still widely held, though I think only by those who have never interested themselves in the histological facts of fracture union, that the union of a fracture of cortical bone is facilitated by accurate coaptation of the broken fragments. This attitude to the union of fractures is equivalent to the accurate coaptation of the edges of skin wounds which is known to be important in plastic surgery. It can easily be shown, however, that callus is never produced from the broken surfaces of bone which are exposed inside the fracture. The broken bone ends are inert until very late in the process of fracture union and all activity takes place in the periosteal and endosteal tissues.

The process of fracture repair involves very great cellular activity and this demands a large blood supply. The blood supply of the broken

ends of a long bone is restricted by the small size of the divided haversian canals and this blood supply cannot increase significantly because of the density of the surrounding bone. The periosteum and the endosteum, on the other hand, being soft tissues, can increase their blood supply and produce a voluminous growth of new tissue with mitotic activity of cell division similar to that of a bone sarcoma.

The circulation in the cortex of a long bone is principally directed in a longitudinal direction, as indicated by the general direction of the haversian canals. These parallel canals connect transversely at intervals with adjacent canals and also with the vessels of the periosteum and endosteum. When the shaft of a bone is fractured the longitudinal circulation must inevitably be interrupted at the site of the fracture. It is obviously impossible to have a "through" circulation in the extreme ends of the bones where the broken haversian canals present directly into the fracture hæmatoma. The circulation in the haversian systems thus proceeds only in the parts where there is a continuous "through" circulation, and this results in the by-passing of the actual bone end which is left as an ischæmic layer on the broken surface.

The existence of this ischæmic surface at the actual broken end of a long bone is clearly revealed in cases where the fracture is infected, because the addition of bacterial toxins seems to render the "death" of the ischæmic portion more complete and there may be difficulty in the dead bone being re-incorporated. This sequence was common in the days of septic amputations, which are really infected compound fractures, and the separation of the sawn end of the bone as a "coronet" sequestrum was well known to the old surgeons. The coronet sequestrum demonstrates the volume of bone rendered ischæmic as a result of interrupting the longitudinal circulation in the haversian systems at the bone ends by the line of the section.

The presence of ischæmic bone ends in long-bone fractures passes quite unsuspected in routine X-rays because there is no difference in the radiological density of the bone end and the living shaft during the time necessary for fracture union. If the X-rays of healing fractures are carefully scrutinized it will frequently be observed that periosteal callus never springs from the bone end and never from the periosteal surface of the fragment exactly at the level of the fracture. The periosteal new bone will be seen to spring from the periosteal surface of the fragment a short distance from the fractured end (Fig. 1). In the same way, the radiological appearance of a cavity will be seen inside the investment of periosteal new bone surrounding the bone ends. That this radiological appearance indicates a true cavity inside the callus can easily be shown when opportunities are available for preparing specimens of fractures in the fourth to sixth week of healing.

It is fairly obvious that any procedure which strips the periosteum from the surface of bones will interfere with this natural process of repair. The stripping of periosteum from the bone surface will deprive the haversian systems near the broken ends of access to blood by lateral anastomoses. The stripping of periosteum will thus increase the volume of ischæmic bone in the fracture and this is the greatest single source of evil in the operative treatment of fractures. In any closed fracture there is always a certain volume of ischæmic bone produced by the fracture, but this volume will be increased by the stripping of soft parts to perform internal fixation.

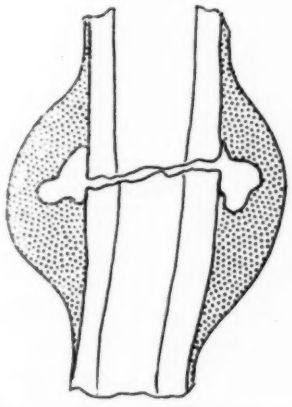

FIG. 1.—Typical distribution of periosteal callus in a closed fracture, showing that the callus never appears from the ends of the fragments.

In connexion with the ill-effect of operative exposure in increasing the volume of ischæmic bone, we see why a slight bacterial infection of a fracture is more serious than a similar slight infection of a soft-part wound. The inoculation of a soft-part wound with a few bacteria puts these organisms in close contact with an active circulation in the soft tissues and there is every possibility that the organisms will be destroyed if they are not violently pathogenic. A small inoculation of organisms lying among ischæmic bone fragments will permit the organisms to multiply in an admirable bacteriological medium without exposure to the circulation which would combat their growth.

The Fallacy of Defective Osteogenesis

A common misconception of the cause of delayed union is the idea that some patients do not produce callus as vigorously as do others. On the contrary, in the case of established non-union it is well known that the bone ends become greatly thickened by new periosteal bone heaped up round the ends of the adjacent fragments. Non-union is not a case of failure to produce new bone; the essential failure seems to be an inability of the new bone to flow across the fracture line to make contact with the new bone from the other side. I do not wish to throw out a misleading analogy, but this failure to unite is not unlike the failure to solder two pieces of metal in the absence of a suitable "flux".

The failure of a fracture to unite cannot be due to systemic or humoral causes because patients with multiple fractures may have some which unite in normal time while others pass to non-union. In the same way, delayed union of the lower third of the tibia is frequently encountered in athletic young men whereas delayed union is not a frequent complication of senile patients. It is possible that this can be correlated with the vascularity of the bones; in senile patients the long bones have large medullary cavities with the bone of the cortex opened up by expanded haversian canals, but in the young athlete the medullary cavity of the lower third of the tibia is very small and the broken bone end presents as a dense piece of ivory with a total area of haversian canals which must be remarkably small.

The failure of callus to cross the gap of a fracture, not the failure to produce callus, is the fundamental problem in fracture repair. A fracture which has trivial displacement invariably unites without difficulty. A fracture with trivial displacement is just as completely broken, as regards the interruption of blood supply in the haversian systems involved by the fracture, as is a fracture with considerable displacement. It would seem obvious that the reason for the ease of repair in undisplaced fractures is that the soft parts, of which the attachment of the interosseous membrane is probably the most important, still bridge the fracture and are able to conduct callus rapidly from one fragment to the other. On the other hand, where there has been gross displacement and gross tearing of the interosseous ligaments and other soft parts connecting the bone ends the pathway for the callus is completely torn. In this case the callus which is produced by the bone ends in adequate quantities for repair is unable to flow across the fracture and heaps itself up round the bone ends.

The Fallacy of Absolute Fixation

It is well known that bones which produce a large mass of investing periosteal callus can unite even in the presence of continuous movement; examples of this are seen in the shafts of the humerus and the femur where the surface of the bones gives rise to muscle fibres and obviously has a very good blood supply. Where the bone is subcutaneous and gives rise to little or no muscle, as in the lower third of the tibia, the production of periosteal callus in large quantities is the exception rather than the rule. It has been customary to imagine that if a bone habitually produces only slight callus the defect is to be remedied by imposing the strictest fixation, in order that delicate strands of callus will not be ruptured by movements of the fragments and made to turn back to become a non-union. I believe this to be one of the most deeply ingrained of all fallacies in fracture treatment. It assumes what is the fundamental problem in osseous union, that at some part of the fracture a delicate strand of callus succeeded in bridging the fracture line and that this strand was thereafter ruptured by movement. If incomplete fixation were to be the main cause of delayed union, the use of metallic internal fixation ought to have shown a very noticeable diminution in the incidence of delayed union, but this is not the case.

If we regard the existence of intact soft-part pathways extending from fragment to fragment as the essential element which conducts callus from one fragment to the other, it is obvious that accurate reduction and absolute fixation will still leave these callus pathways torn and the callus which is produced will heap up round the bone ends and still fail to flow across the fracture.

Initial Displacement

I am thus forced to believe that the most important feature in the union of a fracture is the extent to which the soft parts are torn at the time of the injury. From the degree of displacement it may be possible to hazard a guess at the likelihood of an intact callus pathway existing.

This rather fatalistic approach thus emphasizes that the good results of internal fixation will be obtained in exactly those fractures which would unite well by conservative means. In the same way, cases which would show slow union by conservative means would also show slow union by operative means.

Treatment

From these remarks I would suggest the

following sequence of ideas in the treatment of a fracture of a tibia:

(1) The possibility of an intact soft-part pathway being present from inspection of the original deformity should be assessed. It must be remembered that the first X-ray may not necessarily show the full displacement as sustained at the time of the accident if the deformity has been improved by first-aid measures.

In the case of the tibia those fractures which are likely to have intact soft parts are those in which the main deformity is angulation; fractures in this category are those in which simple correction of angulation will result in a fracture which can be accepted without further manipulation. If the fragments are overriding and correction of angulation is insufficient without further attempts to obtain length and apposition, there is a strong possibility that delayed union will be encountered.

(2) In cases where intact soft parts are present and there is no undue fear of delayed union, the surgeon has available any method which the circumstances may render most attractive. The fracture could be treated in a plaster cast or by internal fixation without plaster with equally good results as regards osseous union.

(3) If the initial displacement is such that rupture of the soft parts makes the possibility of delayed union probable, the fracture must be treated with the main eye to using a bone-graft, of the Phemister type, using iliac bone, at about ten weeks from the time of the injury.

Some surgeons may prefer in these cases to consider a primary bone-graft at the time of the fracture. These may advise metallic internal fixation reinforced with a graft of cancellous bone applied as a sliver to the side of the fracture as a primary procedure. This procedure is logical but there are occasions when the condition of the patient makes it undesirable for it to be undertaken within a few hours of the accident. If the operation has to be delayed the condition of the skin may become unsuitable for internal fixation and many of these fractures are compound.

It is my practice in these cases to treat the tibia conservatively for eight or ten weeks and then, if clinical tests still show readily detectable motion, to proceed without further delay to apply a Phemister bone graft. In this way the most difficult fracture will be soundly united and finally out of plaster within six months from the time of the injury. This sequence eliminates the possibility of devitalizing a greater volume of bone than was devitalized by the fracture itself.

Dr. Donald C. Norris (London):

Summary.—Dr. Norris, who advises insurance companies in dealing with claims for damages for personal injury, said that the interests of the insurer and the surgeon were identical, both desiring early and accurate diagnosis, adequate treatment, and effective resettlement. Patients often lacked proper assistance in getting their claims settled, and surgeons could assist by keeping full and accurate records, furnishing reports, and seeing that the patient had adequate advice on his social, financial and legal problems. He stressed the importance of case conferences with all concerned represented, and discussed details of the rehabilitation organizations involved. In Industrial Rehabilitation Units no significant difference had been found in the results obtained in compensation cases and others. He presented a large number of case histories to illustrate the points he made.

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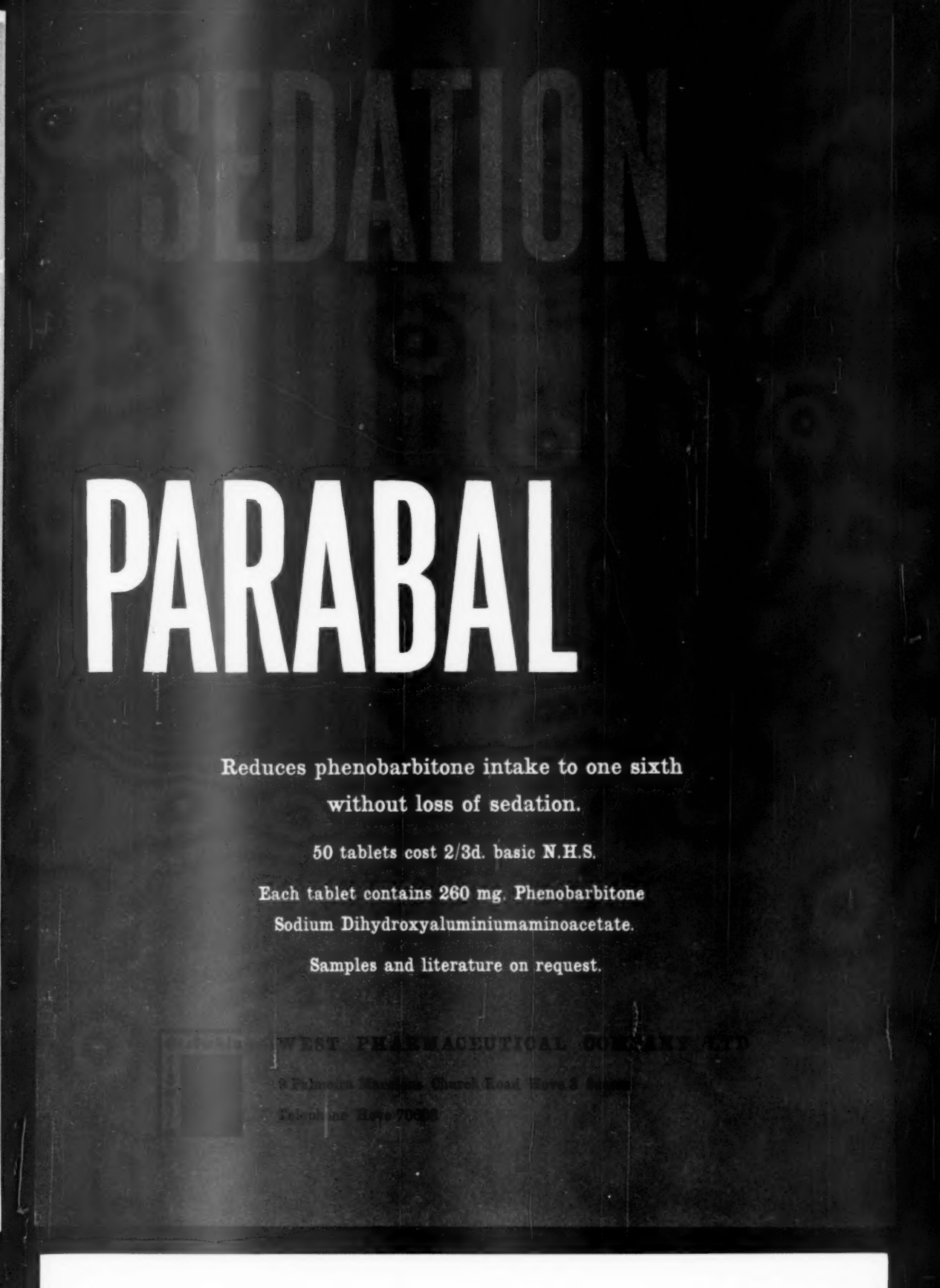
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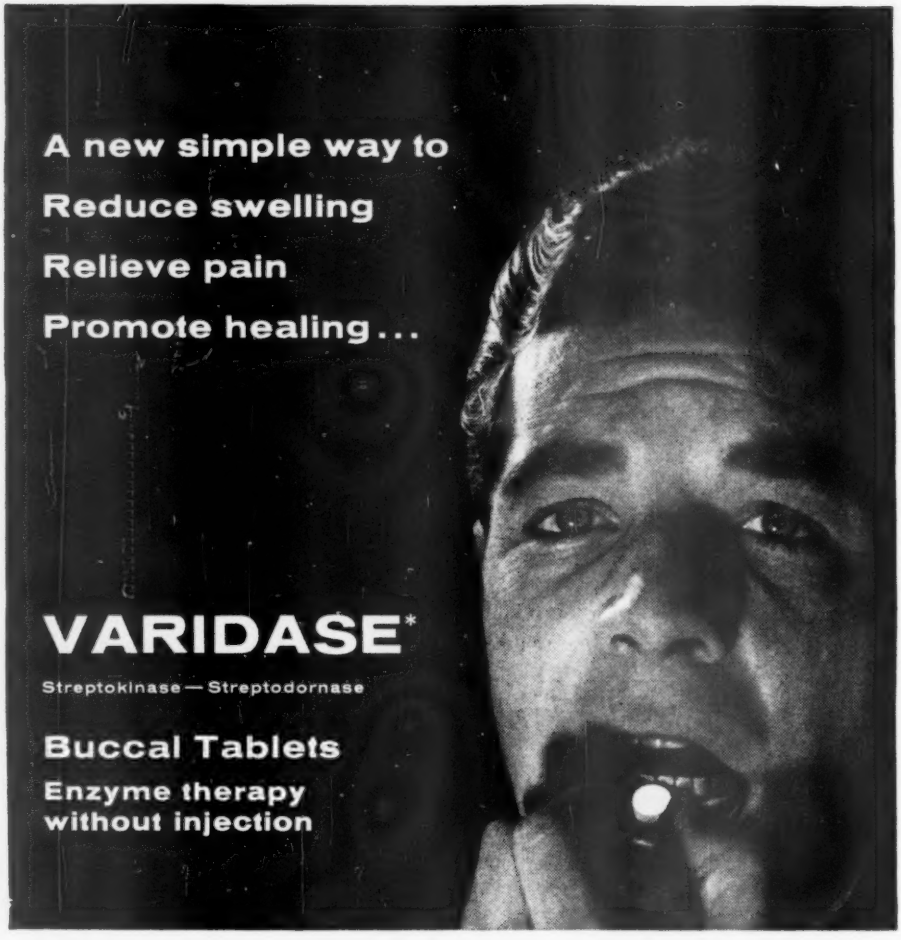

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Meeting
November 28, 1958

Congenital Tuberculosis.—J. M. CASHMAN, M.B., D.C.H. (for J. J. KEMPTON, M.D., M.R.C.P.).

J. T., female, aged 7 months.

A 34-week premature baby weighing 3 lb. 11 oz. at birth; delivery was normal. She was admitted immediately to the premature nursery. Six weeks earlier the mother had had an illness described as Asian 'flu but appeared to have recovered completely.

On the second day after delivery the mother developed a temperature up to 101° F. and dyspnœa. The temperature settled in forty-eight hours but the E.S.R. remained high, 80 mm. in one hour (Wintrobe) and radiograph of the chest showed miliary shadows. There was no sputum. Gastric washings were negative. She was tuberculin positive and was known to have had a calcified primary complex at the age of 12.

There is a strong family history; her father died of pulmonary tubercle, her brother had a pleural effusion and her mother and sister both had tuberculosis.

She was transferred to Peppard Chest Hospital and had fourteen weeks' treatment with isoniazid and streptomycin followed by PAS and isoniazid.

She has made a straightforward recovery and remains under observation.

The baby.—The baby made good progress during her first weeks. Mantoux and a chest radiograph at 2 weeks were negative.

She was 5 weeks and 5 days old when, quite suddenly, she became limp and refused her feeds. The same evening she was dyspnœic, coughing and pale. There was diminished air entry at the right base and enlargement of the spleen and lymph glands in neck and axillæ. No choroidal tubercles were seen. A radiograph of the chest showed impaired translucency at the base of the right upper lobe, the right middle lobe and part of the right lower lobe (Fig. 1).

Gastric washings were positive for tubercle bacilli on culture and guinea-pig inoculation. Mantoux 1/1,000 was doubtful at 6 weeks but she had a positive Heaf test at 9 weeks confirmed by a further Mantoux.

She was started on streptomycin 20 mg./lb. and isoniazid 20 mg. daily.

For the first three days she remained ill and needed oxygen and tube feeding. She ran a low-grade fever for a week. After this she made good progress for a month when she had a series of convulsions. C.S.F. then showed 2 lymphocytes/c.mm. Protein 90 mg./100 ml., sugar and chlorides normal. Culture for tubercle bacilli negative.

She was given phenobarbitone and the

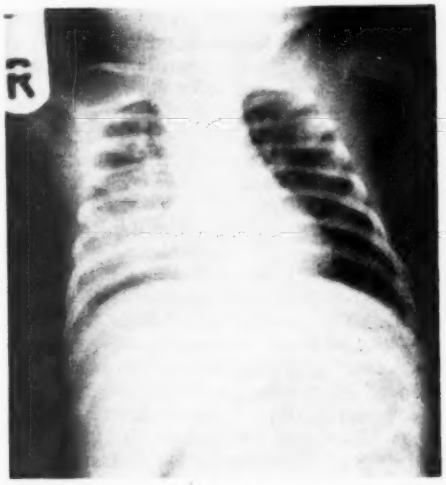

FIG. 1.—Age 6 weeks: Chest X-ray showing impaired translucency in right mid-zone.

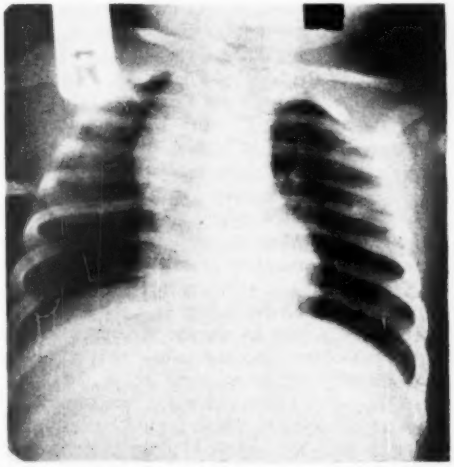

FIG. 2.—Age 6 months: Chest X-ray after 18 weeks' treatment.

isoniazid was reduced to 5 mg. daily as it was thought possible that the comparatively high dose might be toxic.

Since then she has done well. Streptomycin was stopped after three months and she was given isoniazid 10 mg. daily and PAS 3 grams three days a week for three months more. She left hospital on 20.9.58 aged 4 months weighing 13 lb. 12 oz. She is a happy baby and appears to be healthy and developing normally. Her hearing seems to be normal. Chest film shows almost complete clearing (Fig. 2).

Discussion.—In 1935 Beitzke said that in a case of supposed congenital tuberculosis it must be shown that the disease process was tuberculous and that it was present at birth or within a few days or, in cases presenting later, that the primary complex was in the liver or extra-uterine infection was excluded by separation from the mother at birth and segregation from any other possible source of infection.

This baby certainly had tuberculosis, was separated from her mother and developed signs while still in the Premature Baby Nursery. She was never in contact with the father or other possible infectors.

Reported cases of congenital tuberculosis were reviewed by Corner and Brown in 1955. They found 133 cases in the world literature and added another; 3 of these had been treated and survived.

I have found accounts of 11 more, including 4 survivors (Riordan, 1955; Fouquet *et al.*, 1955; Hudson, 1956; Andersen and Fredhjem, 1954; Wayl and Stein, 1958).

Infection in congenital tuberculosis may occur in several ways. There may be hæmatogenous spread from miliary foci in the placenta to the liver when the illness may present as jaundice, or through the ductus venosus giving multiple lesions in the lungs. The liquor amnii may be infected either from the placenta or, after rupture of the membranes, from a tuberculous endometritis. Infected liquor may be swallowed, giving primary infection in the gut, or inhaled, giving a lung primary. It is probable that this was the mode of infection in our case and that, as one would expect in the newborn, there was rapid dissemination of infection giving lymph gland and spleen enlargement.

Congenital tuberculosis is a rare disease but since it can now be successfully treated it should be considered in the diagnosis of atypical respiratory illness or jaundice in the first few weeks. The tuberculin test is not helpful at the onset. Gastric washings should be cultured and the mother X-rayed and, if the diagnosis seems likely, treatment should be started while awaiting bacteriological proof; if it is delayed the baby will die.

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Juvenile Xanthomatosis—Histiocytosis-X.—B. GANS, M.D., M.R.C.P.

B. U., male, born 7.2.58. Only child. No family history of xanthomatosis. Developed (according to his mother almost overnight) five raised, firm, painless, yellowish-pink, damson-sized lesions on his scalp at the age of 6 weeks. Progress before and since the appearance of eruptions has been normal. When first seen, aged four months (Fig. 1), had, in addition to

FIG. 1.

the scalp lesions, flat, reddish-brown, firm infiltrations of indistinct outline on his left arm, right leg, above his right eyebrow, and to the right of his nose. His liver and spleen were enlarged, 6 and 3 cm. respectively, below the costal margins.

A biopsy of a scalp node (Fig. 2) was reported (Dr. M. O. Skelton) as a histiocytoma, a local manifestation of a histiocytosis-X or Letterer-Siwe disease. Serum cholesterol 133 mg.%. Skeletal survey at 4 months and again at 9 months: no bone lesions. Blood count: Hb 65%, W.B.C. 5,500 (polys. 14%, eosinos. 1%, lymphos. 82%, monos. 3%).

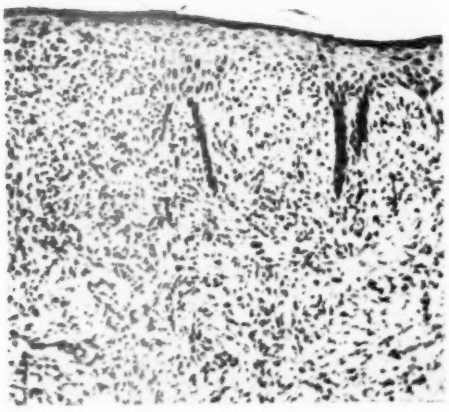

FIG. 2.

Infant started on prednisone on 6.6.58, and still under treatment. For the first three months slow increase, during the last two months steady decrease, in the hepatosplenomegaly. No new skin lesions have appeared, but they have become slightly darker, larger and flatter. Throughout, the infant has made excellent physical and mental progress.

Juvenile xanthoma usually appears shortly after birth and lesions are found mainly on the scalp and face, but also on the limbs and occasionally the trunk. In contradistinction to the tuberous, the disseminated and the secondary xanthomatoses, the serum lipid levels are normal in these children. Whereas in most xanthomatoses a very similar histological picture underlies a diversity of clinical syndromes, the opposite holds for juvenile xanthoma. Histologically, the skin lesions may resemble histiocytoma, dermatofibroma, nævo-xantho-endothelioma, or sarcoma cutis (Weber, 1908; McDonagh, 1909, 1912). The variegated histological picture may be due to changes occurring in the lesion as it ages. At the beginning the cutis is stuffed with histiocytes and there are few giant cells. At this stage no lipid is found. Later on lipid material is taken up and the histiocytes change to foam cells and the number of giant cells increases.

In this case of juvenile xanthoma there is evidence of systemic involvement, as shown by the hepatosplenomegaly. Lamb and Lain (1937) described a case of juvenile xanthoma with pulmonary infiltration and Blank *et al.* (1949) a similar case with ocular involvement. Most writers now agree with Tannhauser (1950) that juvenile xanthoma should be grouped between the hypercholesterolæmic disseminated xanthomatoses and the normocholesterolæmic "Histiocytosis X" of Lichtenstein (1953) (Table I).

TABLE I.—GENERALIZED XANTHOMATOSES

Primary Xanthomatoses	
Tuberous	
Disseminated	
Juvenile	
"Histiocytosis X"	
Letterer-Siwe	Normocholesterolæmic xanthomatoses
Hand-Schüller-Christian	
Eosinophilic granuloma	
Cerebroside reticulosis	
Gaucher's	
Sphingomyelin reticulosis	
Niemann-Pick	
Secondary Xanthomatoses	
Diabetes mellitus	
Hepatic cirrhosis	

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Two Cases of Subacute Inclusion Body Encephalitis (Van Bogaert's Encephalitis).—JOHN RENDLE-SHORT, M.A., M.D., M.R.C.P., D.C.H.

Case I.—John, an illegitimate boy aged 4 years and 1 month, was well until six days before admission when his sleep became poor. While chasing his sister he ran into the washing machine and cut his eye. Next day he fell and hit his face again. After that he was constantly falling.

On examination.—There were frequent akinetic seizures with sagging at the knees. If he were running these would cause him to fall. Apart from bruises there were no other abnormal physical signs.

Investigations.—All normal except for: C.S.F.: W.B.C. 1 per c.mm., protein 40 mg. per 100 ml., Lange 5554321000. EEG (Fig. 1): slow activity with periodic diphasic complexes. Appearance consistent with Van Bogaert's encephalitis.

Progress.—The child became stuporous and after a few days developed myoclonic jerks. These occurred about every six seconds and involved different parts of the body; sometimes the legs, sometimes the arms or the head predominated. In addition the child had a coarse tremor. After a few months the stupor increased and he became comatose. By this time the jerks had become less frequent and he lay in the position of decerebrate rigidity with considerable

FIG. 1.—EEG showing typical complexes. Bottom tracing is of a simultaneous electromyogram of right quadriceps.

opisthotonos. He died three and a half months after admission.

Case II.—Josephine, aged 8 years, developed a cough two weeks before admission to hospital and her memory became impaired. Five days before admission she developed fever, and fell frequently. On the day of admission she had three major convulsions. There was no family history of epilepsy.

On examination.—The child was semi-conscious and showed evidence of gross weight loss. There were no other abnormal physical signs.

Investigations.—She continued to deteriorate mentally and developed myoclonic jerks. These increased in violence for some months and then subsided as she sank into coma. Weight loss was extreme and the child developed a spastic quadriplegia in extension. She died six months after admission to hospital.

[Both cases were illustrated by a film.]

Aûtopsy.—Apart from bronchopneumonia, abnormal findings at post-mortem examination in both cases were limited to the nervous system. The brain macroscopically showed degeneration of the white matter with occasional cysts. Histologically there was gliosis and demyelination, and perivascular infiltration by lymphocytic and plasma cells. Inclusion bodies were quite numerous in Case I but scarce in Case II.

Comment.—Dawson (1933, 1934) and Van Bogaert (1945) described cases which on histological grounds were probably of virus ætiology, but which clinically resembled degenerative neurological lesions. Foley and Williams (1953) have reviewed the subject. The condition occurs in older children and adolescents and there are usually three stages. In Stage I the child has psychic changes, loss of memory, temper tantrums, &c., and develops what appear to be akinetic seizures. This stage lasts three or four weeks. In Stage II the mental deterioration becomes more marked and the child lapses into stupor. At the same time myoclonic jerks develop in which he suddenly moves his limbs, head or trunk. These movements may be very violent. They occur with striking periodicity often at about every 6 seconds, but cease during sleep. In Stage III the movements become less in amplitude and frequency, but the child sinks into coma. Spastic quadriplegia develops often accompanied by opisthotonos and decerebrate rigidity. The total duration of the disease is variable, but six months is usual from onset to death. Some cases in Stage III have languished on for several years. No treatment has yet proved of any avail. No virus has ever been isolated.

Acknowledgments.—I would like to thank Professor R. S. Illingworth for permission to show these cases, the photographic department of the Sheffield United Hospitals for the film and Dr. J. L. Emery for the pathology.

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Non-adrenal Female Pseudo-hermaphroditism Associated with Hormone Administration in Pregnancy.—HUGH JOLLY, M.D., M.R.C.P., D.C.H.

K. J., female, aged 4 months.

This patient is shown to illustrate recent evidence (Hayles and Nolan, 1958; Moncrieff, 1958; Nellhaus, 1958; Wilkins *et al.*, 1958) emphasizing possible dangers to the developing fœtus from the administration of hormones in pregnancy.

First child. One previous miscarriage. During pregnancy a threatened miscarriage occurred at 3 weeks and intermittent vaginal bleeding continued to the 14th week. For this reason progesterone (Progestin) was given intramuscularly to the mother, starting with 5 mg. every third day from 3½ weeks, increasing to 25 mg. daily at 6 weeks and continuing with this dose until the 17th week of pregnancy. Total dose 4,080 mg. Two 100 mg. implants of progesterone were also administered but it is doubtful whether either of these had much effect as the first sloughed out and the second is still palpable. Pregneninolone (ethisterone) also given by mouth starting with 60 mg. daily at the 7th week and increasing to 120 mg. daily by the 17th week. From this time the dose was gradually decreased and was stopped shortly before delivery. Total dose approximately 21,000 mg. Pregnancy was otherwise normal except for a two-day bout of influenza at the 16th week.

The baby was born at term, weighing 7 lb. 2 oz. and was normal except for enlargement of the clitoris and labia. Two spots of vaginal bleeding occurred on the first and fourth days but no breast enlargement took place.

Examination at the age of 10 weeks showed a healthy-looking baby with a moderately

FIG. 1.

enlarged hard clitoris while the labia majora were slightly enlarged (*see* Fig. 1). Urethral and vaginal orifices separate. Serum electrolytes normal. Nuclear sex (polymorphs)—female pattern. 17-ketosteroids 1·1 mg. in twenty-four hours. Pregnanetriol 0·03 mg. in twenty-four hours. Bone age normal.

The child is now aged 5 months and the clitoris is much smaller and only a little larger than normal.

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? Thrombotic Thrombocytopenic Purpura.—JOHN LORBER, M.D., M.R.C.P., and JOHN L. EMERY, M.D.

R. H., male, born 18.6.55. First seen at hospital at the age of 2½ years, suspected of tuberculous meningitis following a week of vomiting, lifelessness, drowsiness, increasing pallor and loss of weight. Two weeks prior to this he had had acute tonsillitis for a week which had been treated with sulphadimidine.

On admission.—He was afebrile, but dehydrated, emaciated and very pale. He had neck stiffness, a positive Kernig's sign and three small bruises on his legs. The liver and spleen were not palpable. There was no jaundice or œdema. Blood pressure 125/85. Capillary fragility (Hess) test negative.

Hb 6 g.%, R.B.C. 2,000,000, W.B.C. 20,500 with 2% myelocytes and 2% metamyelocytes. Platelets 90,000. Three days after admission the reticulocyte count was 9%. The bone-marrow was hyperplastic, showing active erythropoiesis. The serum contained a high blood urea (126 mg.%), hyperbilirubinæmia (3·4 g.%, delayed direct positive), hypoproteinæmia (total 4·2, albumin 2·4 g.%) and hypercholesterolæmia (370 mg.%). The urine contained less than 10 mg.% of albumin, 50 to 60 R.B.C. and 10–12 W.B.C. per high power field. There was no excess of urobilinogen on several examinations. The C.S.F. was normal.

Course of disease after admission.—For nine days he was investigated without any drug treatment or blood transfusions. Vomiting and anorexia persisted, and he lost 350 grams in weight. There was no evidence of infection or of clinically detectable jaundice. There was no further fall in hæmoglobin level. The total and differential white cell count returned to normal, but the reticulocytes rose to 21%.

The serum bilirubin fell from 3·4 mg.% and gradually returned to normal. The serum proteins fell to 3·7 g.% resulting in clinical œdema. Albumin appeared in his urine seven days after admission (350 mg.%) and persisted for one week. The blood urea steadily fell as the dehydration was corrected.

Serological tests.—Group O, Rh-positive. Coombs test negative. Weak auto- and pan-agglutinin at 4° C. Acid hæmolysin test negative. No Rhesus or Kell antibodies. From these results it was concluded that there was no serological evidence of an acquired hæmolytic anæmia of the auto-immune type.

Treatment.—On the ninth day he was given a transfusion of 300 ml. of packed cells which was followed by improvement in his general condition in spite of a steady drop in the hæmoglobin level to 7·7 g.% a week after transfusion. The very low platelet count persisted and fresh petechiæ appeared in the mouth, more spontaneous bruises developed on his legs and œdema of his face and legs was now very obvious. From the sixteenth day of admission he was treated with 300 mg. of cortisone daily for two days, 200 mg. daily for four days followed by 100 mg. daily. There was gradual improvement in his condition; he stopped vomiting, the petechiæ and œdema disappeared and his hæmoglobin rose slowly to normal four weeks after starting treatment. The platelet count, the reticulocyte count and the serum proteins rapidly returned to normal. Cortisone was given in smaller doses and discontinued after five weeks. There was no clinical or hæmatological relapse and he remained symptom-free to-date, seven months after his admission.

Capillary microscopy was performed in the acute and in the convalescent stage of the disease. The capillaries of the nail beds appeared to be abnormal both in form and size. They had irregular loops and appeared compound. They sometimes had accessory large loops and anastomosing loops (Fig. 1). The most remarkable feature, however, was that some of the loops were grossly enlarged, and the blood in them at first sight appeared completely stationary, while the blood was circulating normally through surrounding capillaries. The blood in these large stagnant loops was not clotted, as after a period of time a small amount of movement appeared to take place when examined for any long period. This feature of stagnation in abnormally large loops was most prominent in the acute stage and was still present to a lesser degree four months afterwards.

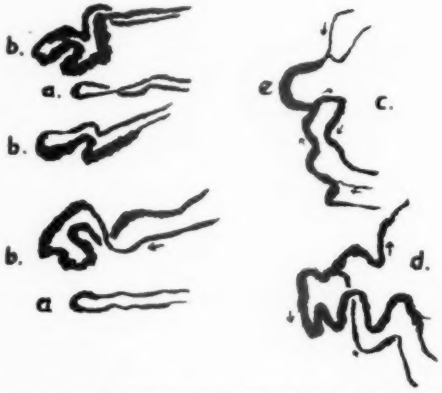

FIG. 1.—Drawings of capillary loops in the skin at the root of the nail bed. Arrows indicate direction of blood flow. (*a*) Normal capillary loop (approximately 50% of loops). (*b*) Dilated and tortuous loops through which the blood passes extremely slowly. These loops do not appear to be dilated normal loops. (*c*) and (*d*) Abnormal loops showing a picture more like a subcapillary plexus, but throwing up dilated loops such as in (*e*), in which the blood appears to be stationary. Drawings (*c*) and (*d*) are at a slightly lower magnification than (*a*) and (*b*). It would seem possible that the thrombotic lesions occur in the loops (*e*).

Discussion.—This case seems to fit in with the description of thrombotic thrombocytopenic purpura, or thrombotic micro-angiopathy (Symmers, 1956). The four cardinal clinical features of this condition, according to Symmers, consist of a febrile illness of hæmolytic anæmia with a negative Coombs test, associated with thrombocytopenic purpura and a variety of neurological symptoms, which in our case consisted of meningism. Another common feature is renal involvement. The previously described cases, of which approximately 100 had been reported, all occurred in adolescents or adults and were invariably fatal. In this respect the present case differed and as there is no histological proof of the basic lesion, namely micro-aneurysms of the small vessels throughout the body, the diagnosis cannot be considered conclusive. Some support, however, was obtained by capillary microscopy. Allison (1957) described a group of 6 infants of whom 4 survived. They probably represent an infantile form of thrombotic micro-angiopathy. In the 2 infants that died, platelet thrombi were found in small blood vessels. In the surviving infants there had been no neuropathy, and thrombocytopenia was not constant.

Our case appears to be more like the adult cases surveyed by Symmers, and we feel that it represents a juvenile form of the condition. It is not possible from this one case to assess the

diagnostic value of the form of the capillaries in this condition, but the examination would seem useful in suspected cases.

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Galactosæmia: Cerebral Hæmorrhage While on a Galactose-free Diet.—J. D. SHEWARD, M.D., M.R.C.P. (for I. M. ANDERSON, M.D., F.R.C.P.).

L. S., female, born 21.3.58. Age 8 months.

Family history.—Healthy parents. Both have normal galactose tolerance curves. There is no family history of a bleeding disorder. No siblings.

History.—Normal delivery, after an uneventful 38-week pregnancy; weight 5½ lb. She did not thrive on adequate quantities of breast milk. There was an episode of diarrhœa and vomiting at 7 weeks. She had never been jaundiced. At 9 weeks she weighed 6 lb. 2 oz. and because of her failure to thrive she was admitted for investigation.

On examination.—A thin child with no abnormal signs. The liver was not enlarged and there were no cataracts.

Investigations.—Hb 10·5 g.%, W.B.C. 6,000. Urine: No cells, casts or albumin. Benedict's test positive (green precipitate). The reducing substance was identified as galactose, chemically and by paper chromatography. Paper chromatography of desalted urine for amino acids showed spots of glycine, serine, taurine, glutamine, histidine and proline.

Blood galactose levels after 3 grams of oral galactose (50 mg. per lb.):

Fasting	½ hour	1 hour	1½ hours	2 hours	
0	62	51	46	33	mg.%

Galactose index: 192 (normal = less than 160).

Blood chemistry.—Sodium 143, chloride 109, alkali reserve 17 mEq./l. Blood urea 8 mg.%. X-ray chest normal; no osteoporosis.

Progress.—She gained weight rapidly on a lactose-free diet (Nutramigen). She developed normally and there were no symptoms until her second admission.

Second admission at 5 months old, having been on Nutramigen for two months. She had been ill for 1 day, during which she vomited, refused feeds and became progressively unresponsive. Small bruises had appeared on the face and legs.

On examination.—Temperature 99° F. Acutely ill, pale, lethargic, unresponsive infant, with bulging anterior fontanelle, left III and VII nerve palsies and right hemiparesis following right-sided convulsions. Three small bluish spots on the face and thighs. Spleen just felt. Liver not enlarged. Optic fundi normal.

Investigations.—C.S.F. xanthochromic, blood-stained. Prothrombin time 180 sec. (control 14 sec.). Hess's test negative. Platelets normal. Hb 8·0 g.%. W.B.C. normal. Alkaline phosphatase 26 K.A. units. Other liver function tests normal. Alkali reserve 16 mEq./l.

Progress.—She developed increased intracranial pressure, with arterial hypertension, blood pressure 160/90, bulging fontanelle, apnœic periods and further convulsions. Subdural and ventricular taps through sutures and left burr hole showed bleeding over and within brain and cerebral œdema. Treatment with anti-convulsants, antibiotics, cortisone, magnesium sulphate, intravenous hypertonic saline, blood and oxygen. Four hours after vitamin K 5 mg. intramuscularly the prothrombin time was 40 sec. (control 15 sec.). A day later, the prothrombin time was normal. Following a period of decerebrate rigidity lasting two weeks, consciousness returned after five days. At eight months she shows slight spastic weakness of right arm and leg but no retardation. She continues to gain on a lactose-free diet.

Discussion.—In galactosæmia hæmorrhage is sometimes a feature. In a report of 6 cases by Cox and Pugh (1954) bleeding occurred in 2: one died from a cerebral hæmorrhage and had a hæmatemesis. The other bled from the umbilicus on the tenth day. Clay and Potter (1955) reported an infant with galactosæmia who passed blood in the stools on the ninth day of life. Holzel (1958) reports the finding of a cerebral hæmorrhage in a galactosæmic infant, who later died of liver failure and complete biliary obstruction. Donnell and Lann (1951), in a study of 4 cases, found areas of hæmorrhage in the pancreas of an infant who died at 4 weeks of age.

In the cases cited above, there was either clinical and laboratory evidence of severe liver dysfunction, or autopsy evidence of hepatic cirrhosis. None of these infants was receiving a lactose-free diet. Thus a bleeding tendency appears to be a manifestation of severe, untreated galactosæmia with extensive liver damage.

The present case is unusual in that a cerebral hæmorrhage occurred in one showing little clinical or laboratory evidence of disturbed liver function, while the patient was on a lactose-free diet and in which the degree of galactosæmia had previously been shown to be mild. In addition, this infant showed a persistently low alkali reserve, an unexplained feature of the disease that has been noted by Arthurton and Meade (1954). The cause of the bleeding remains conjectural. Initially there was evidence of hypoprothrombinæmia, which was quickly corrected by vitamin K administration. Extensive liver damage, of which there was scant evidence in this case, may lead to a sufficient lowering of prothrombin to cause bleeding. There were no indications of any factor, such as intestinal hurry, absence of bile salts, or alteration in the intestinal bacterial flora, which might have impaired the absorption of vitamin K. An intracerebral vascular anomaly has not been ruled out, but a connexion between galactosæmia and cerebral hæmorrhage appears likely.

While bleeding appears to be uncommon in treated infants, neurological disturbances have occurred in patients on lactose-free diets. Convulsions occurred in Clay and Potter's patient, two months after starting the diet. One of Cox and Pugh's patients had fits while on treatment. Choreiform movements were reported by Goldbloom and Brickman (1946). The early dietary treatment of galactosæmia is curative for the majority of affected infants, although unexplained deaths may occur according to Komrower (1957). The experience of the present case and others shows that there are occasional serious complications and deaths in spite of treatment.

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Dwarfism ? Cockayne ? Russell Type.—O. P. GRAY, M.R.C.P. (for P. R. EVANS, M.D., F.R.C.P.).

History.—V. L., female, born 17.3.55. Present age: 3 years 8 months.

Mother, aged 26, well. Father, aged 29, well. No consanguinity. First child born in 1952, full-term, normal pregnancy and delivery, birth weight 4½ lb. The appearance was similar to that of the present patient. Died aged 8 months from meningococcal septicæmia.

Mother then had two miscarriages, followed by the patient, and now has a normal son, aged 18 months.

Birth weight: 3 lb. 13 oz. Pregnancy: full-term by dates.

Both mother and doctor thought uterus small for dates. Mother noted fœtal movements were weak. She had vaginal monilial discharge, but no bleeding. The placenta was small and infarcted. The child's peculiar features were noted shortly after birth. She had reddish brown discoloration of the buttocks at birth which lasted for several weeks and disappeared spontaneously. She was difficult to feed and rarely took more than 2 oz. She still has a poor appetite and gains weight slowly. Occasional cough and looseness of the motions. Recently is a little deaf. Father has some brothers who are deaf. Milestones at normal time.

On examination.—Weight 17 lb. (mean 32 lb). Height 31 in. (mean 38½ in.). Sitting height 19½ in., span 27¾ in. (mean 36 in.). Head circumference 19¼ in. (=mean). Birdlike in appearance and behaviour. Features petite, head triangular—large compared with the rest of body. Deepset eyes—pointed "beaky" nose —small chin—ears set far back. High arched palate. Arms, hands and feet disproportionately short. Digital clubbing. Fundi normal. Blood pressure 90/60. Hyperextensible joints except elbows (Fig. 1).

FIG. 1.—V. L., aged 3 years 8 months, showing dwarfism with bird-like features, disproportionately short arms, and small hands and feet.

Investigations.—Hb 70%. Film suggests iron deficiency. Urine: traces of lactose. Sweat test negative. Serum electrolytes normal. Urea 32 mg.%. Total proteins: albumin 3·2, globulin 3·0 grams%. Electrophoresis: moderate reduction of the gamma globulin. X-ray skull normal; no intracranial calcification. Urine: chromatogram for amino acids and indoles negative. Bone age 21 months. Insulin glucose tolerance test showed prolonged hypo-glycæmia. W.R. and Kahn negative.

This girl shows some features of both the Cockayne and the Russell type of dwarfism. Her petite build and features with the active nimble movements immediately suggest the description of "birdlike"—a term used by Cockayne (1936, 1946) when describing his dwarfed patients. The sunken eyes and maxillary prognathism are like the Cockayne type (Neill and Dingwall, 1950). On the other hand the normal head circumference and the high bossed forehead are more in keeping with the Russell type. The nose is long and prominent and slightly beaked at the tip. This is seen in both types as is the receding jaw. The mouth shows a little of the inverted V configuration described by Russell (1954) but this child's is no more than in many normal children. She does not show the overlapping of the upper over the lower lip seen in Russell's case. The high arched palate, which this child has, was also noted by Cockayne.

The general body configuration with disproportionately short upper limbs, small hands and feet is seen in the Russell type. The Cockayne cases had relatively big hands and feet with long legs. These children also had normal birth weights whereas the present patient was small at birth, and the uterus was small throughout the pregnancy. The placenta was recorded as infarcted by the nurse and thought to be small by the mother—features noted in the Russell type.

A recent development in this child is the onset of early deafness. This was well marked in the Cockayne dwarfs when first seen at the age of 6 and 7 years. At that time they were considered to be a little below the average in intelligence although as the years went by they became much retarded with a small head. The present patient appears to have a normal development quotient. An interesting finding in this child is the impaired response to hypoglycæmia. This may be related to the retardation in bone age and suggest an element of pituitary deficiency. Russell also noted an impaired hypoglycæmia response and Cockayne noted an unusually small pituitary fossa in his cases.

A unique feature appears to be the presence of hypogammaglobulinæmia. It could be related to the recurrent episodes of minor chest infection which this child has. The sister, who was similarly affected, died from the Waterhouse-Friderichsen syndrome. It is possible that this girl also had hypogammaglobulinæmia and her poor response to infection could well be related to this.

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Cardiac Angina Due to Rheumatic Aortic Incompetence, Treated by Suture of Aortic Valve Cusps.—R. C. ROXBURGH, M.D., M.R.C.P., and JOHN JACKSON, F.R.C.S. (for N. M. JACOBY, M.R.C.P., and T. HOLMES SELLORS, M.CH., F.R.C.S.).

T. M., male, aged 12 years.

History.—Apparently well until the age of 7 years when he had the first of five attacks of rheumatic fever with carditis. During the past few years he has developed cardiac enlargement, and severe cardiac angina, at rest and on exercise. Treated in Cyprus and in Turkey without avail, and was advised to come to London for treatment. The pain began in the left mammary region, travelled up to the left shoulder and down the left arm. During attacks lasting about ten minutes he was pale, quiet and sweating profusely.

On examination (Queen Elizabeth Hospital, 30.8.57).—Weight: 55 lb. Anxious facies with mitral flush, gross neck pulsation and visible shaking of body at each heart beat. Cardiovascular system: Radial pulses, collapsing. Blood pressure 115/0 left arm. Heart: precordial systolic thrill. Apex beat in sixth left intercostal space in anterior axillary line, heaving cardiac impulse. Heart sounds: loud systolic and diastolic murmurs present at mitral and aortic areas, characteristic of mitral and aortic valve disease. Spleen enlarged 2 fingerbreadths.

Investigations.—Chest X-ray: "A huge heart, with a normal pulmonary vascular pattern, aortic knuckle on the left side." ECG: "left ventricular strain, but no evidence of ischæmia." Hb 90% (13·3 grams%). E.S.R. 2 mm. in the first hour. W.R. and Kahn negative.

Progress.—Whilst in hospital for observation, continued to have frequent severe attacks of angina at rest, especially at night; there was great distress and anxiety, with sweating and tachycardia. No improvement with any of the

nitrite group of drugs: the only drug which alleviated his symptoms was morphia. On 21.10.57 lesions of erythema marginatum appeared on the trunk.

Treatment.—In view of the bad prognosis on medical treatment alone, Mr. Holmes Sellors agreed to attempt surgical treatment.

Operation (Middlesex Hospital 4.12.57).—General anæsthesia and hypothermia. Exploration of the aortic valve. The aorta was incised above the valve level and the cusps were examined under direct vision. The right cusp showed signs of old rheumatic infection; the posterior and antero-lateral cusps were sutured to reduce the size of the orifice and the aortic wall was closed with a continuous suture. The total time of anæsthesia and hypothermia was three and a half hours, and the time of vascular occlusion was four minutes at a temperature of 30·6° C. (87° F.). Following operation the blood pressure was 140/40–50.

Follow-up.—Since operation, he has had no angina. The physical signs in the cardiovascular system remain grossly abnormal. The heart size on X-ray has diminished. The blood pressure is now 145/60. He has excellent exercise tolerance. He is kept on penicillin V continuously. He has gained 6 lb. (2·7 kg.) in weight. The ECG has shown marked improvement a year after operation, the signs of left ventricular strain have disappeared and the complexes have returned to normal.

Comment.—This patient has been shown on account of the dramatic relief of angina obtained by surgical narrowing of the aortic valve orifice. Angina is a rare symptom in children with heart disease, and in aortic disease angina is much more commonly associated with stenosis than with regurgitation (Wood, 1952). The reason for this is that the mean intra-aortic pressure is lower in most cases of stenosis than in regurgitation and it is the mean pressure which maintains the coronary circulation. It was fortunate for this child that only one of his aortic cusps was diseased (*see* Fig. 1); but for

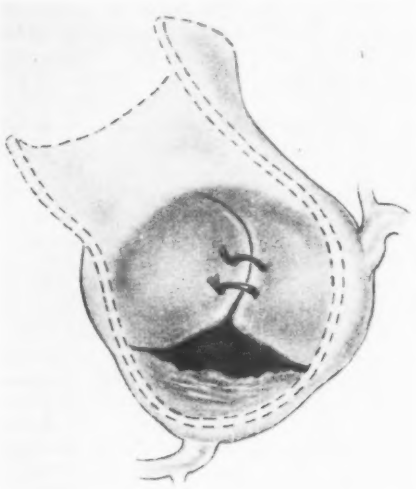

FIG. 1.—Drawing made at the end of operation showing the aortic valve cusps; the two healthy cusps have been sutured together and the diseased cusp lies free.

this, it would not have been possible to narrow his aortic orifice by suture of cusps. Other procedures would have been necessary, e.g. diminishing the diameter of the aorta with a constricting ligature (Taylor *et al.*, 1958). The use of indwelling plastic valves has been disappointing in the treatment of severe aortic regurgitation.

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A case of **Hepatoblastoma with Recovery** was shown by Dr. A. J. HARBOTT (for Dr. D. MORRIS) and a full account will be published elsewhere.

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Clinical Section

President—Sir ERIC RICHES, M.C., M.S., F.R.C.S.

Meeting
December 12, 1958

Dermatomyositis and Bronchial Carcinoma.—OLIVER GARROD, M.B.E., M.D.

A. B., male, 61, engraver.

History.—Raynaud's phenomenon from 1936 to 1939. In 1950, onset of classical discoid lupus erythematosus of face, successfully treated with mepacrine in 1952 (Dr. Peter Borrie). Late in August 1958, bridge of nose and eyelids became red and swollen. One week later he developed a diffuse erythema of face, neck, shoulders, arms and upper chest after a day in the sun. Both upper arms and elbows became swollen, the limbs felt weak, and there was severe difficulty in swallowing, followed by a cough with purulent sputum. On 16.9.58 he was admitted to Barnet General Hospital.

On examination.—Temperature 102·5° F., pulse 120, respiration rate 32. An ill-looking, wasted man, with a diffuse desquamating erythema of face, neck, upper trunk and arms, and telangiectasia of nail beds. Both arms and elbows were greatly swollen and tender. Tissue-paper scars were present on the left cheek and right forehead.

Chest movement and air entry were diminished on the right side, with pleural friction. Blood pressure 180/90. Liver and spleen not enlarged. Neurological examination revealed bilateral weakness of facial muscles, arms and legs, with feeble or absent deep reflexes and wasting of the lower limbs.

Investigations.—Urinalysis: Moderate proteinuria, a few granular casts, no sugar.

Blood: E.S.R. 10 mm. in one hour (Westergren); Hb 106%; W.B.C. 9,500 (neutros. 91%, lymphos. 5%, monos. 2%, myelos. 2%); no L.E. cells.

Sputum: No malignant cells or tubercle bacilli.

Urinary creatine: 380 mg. per twenty-four hours (creatinine 720 mg.).

Serum proteins (electrophoresis): Albumin 3·9, alpha-1 globulin 0·44, alpha-2 globulin 1·32, beta globulin 0·88, gamma globulin 0·88 grams/100 ml.

ECG: Generalized flattening of T waves.

Chest X-rays: 16.9.58, patchy consolidation of right mid and lower zones, rounded mass at right hilum. 23.9.58, slight flattening of right chest, and tracheal shift to right. Previous changes persistent, appearances suggested bronchial carcinoma.

Bronchoscopy 2.10.58 (Mr. R. Laird): Mucosa of both main bronchi inflamed and thickened. Right upper lobe bronchus stenosed, appearances suggest underlying neoplasm. Blind biopsy at this site showed non-specific inflammatory changes.

Muscle biopsy (left biceps, 9.10.58) showed numerous necrotic cells within the muscle substance, with a granular eosinophilic cytoplasm. Sarcolemmal sheath and endomysium intact. No inflammatory cell infiltration. The appearances were those of a polymyositis with inflammatory reaction possibly masked by steroid therapy.

Electromyography (Dr. K. W. Heathfield and Dr. E. Campbell): (1) Right quadriceps: reduced interference pattern of normal amplitude, short duration spike potentials. (2) Right deltoid: patches of typically myopathic pattern, low voltage. (3) Right triceps: large short duration potentials.

Findings supported diagnosis of dermatomyositis.

Progress and treatment.—Fever, dysphagia and skin changes persisted four days and were then relieved in a few days by prednisolone 40 mg. per day. The cough subsided with tetracycline. Creatinuria and proteinuria ceased. He has remained well on a maintenance dose of prednisolone 5 mg. t.i.d. and tetracycline 250 mg. b.i.d., and his muscle strength has greatly improved. The deep reflexes have returned. Further chest X-rays on 24.10.58 showed increased mediastinal shift to the right, further collapse of the right lower lobe, and a small right basal effusion, and on 9.12.58 an increase in the size of the right hilar mass.

The probable bronchial carcinoma was considered to be inoperable, and deep X-ray treatment contraindicated on account of the general condition, absence of chest symptoms,

and excellent response of the dermatomyositis to steroid therapy.

Comment.—The successive occurrence of lupus erythematosus and dermatomyositis in the same patient is exceptional.

The high incidence (10–15% of cases) of carcinoma in dermatomyositis was first reported by Scheuermann (1951) and has been confirmed by Dowling (1955) and others. The carcinoma usually precedes the onset of dermatomyositis, as in this case.

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Carcinoma of the Ureter and Carcinoma of Bronchus.—R. J. RYALL, F.R.C.S. (for Sir ERIC RICHES, M.C., M.S., F.R.C.S.).

Male aged 67, Maltese. Admitted 15.9.58.

History.—1953: Onset of painless hæmaturia lasting for a few days, clearing up spontaneously and recurring at six-monthly intervals till the time of his admission.

1954: Left lower lobe lobectomy by Sir Clement Price Thomas for squamous cell carcinoma of left lower lobe bronchus with a good recovery.

1957: Cystoscopy, said to have shown "varicose veins" of the bladder, was followed by profuse hæmorrhage needing cystotomy for its control.

April 1958: A mass which developed in the suprapubic scar was excised; biopsy showed transitional cell carcinoma. Cystoscopy at this time revealed multiple papillary growths in the bladder.

June 1958: Excision of glands which appeared in right inguinal region showed secondary deposits from transitional epithelium.

August 1958: A mass of glands appeared in the left inguinal region. These slowly increased in size.

On admission.—A well-nourished man. General condition good. Scars of previous operations soundly healed. Non-tender palpable right kidney. Mass of mobile hard glands, size of orange in left inguinal region. No clinical evidence of recurrence of bronchial carcinoma.

Investigations.—Intravenous pyelogram: The right kidney did not excrete. The left kidney excreted at five minutes and was normal. *Cystoscopy:* The right ureteric orifice was obscured by a sloughing growth. Two further papillary growths on base and above left ureteric orifice. Biopsy of these growths showed Grade 1 papillary transitional cell carcinoma. *Right ureteric catheterization:* After preliminary cystodiathermy the right ureter was catheterized. All catheters were held up at 4 cm. *Right ureterogram:* Dye refluxed to bladder.

Management and clinical course.—24.9.58: Right nephro-ureterectomy. The ureter was distended and filled with necrotic growth (Fig. 1).

FIG. 1.—Specimen of nephro-ureterectomy showing carcinoma of middle third of ureter with atrophic hydronephrosis of kidney.

The ureter was adherent to the iliac vessels. Section showed invasion of the ureter by a transitional cell carcinoma with extensive squamous metaplasia. The renal substance showed chronic pyelonephritis.

10.10.58: The mass of left inguinal glands was excised completely. Section of glands: Transitional cell carcinoma, similar to that on the right side.

Cystoscopy (5.11.58): Only one tumour was visible, near left ureteric orifice. It was diathermized to complete destruction. The intramural right ureter was diathermized.

9.11.58: Anuria developed. The left ureteric orifice was obstructed by intramural œdema.

Following catheter drainage of the left kidney for five days, normal micturition was re-established.

Subsequently, convalescence progressed smoothly and the patient was discharged home.

Comment.—This case is of interest for the following reasons: (1) The occurrence of two primary malignant growths in the one patient. (2) The diagnosis of carcinoma of the genito-urinary tract was first made by biopsy of a secondary deposit in the abdominal wall. (3) The danger of implantation of papillary growths of the bladder in the wound of approach. (4) The necessity of carrying out nephro-ureterectomy for tumours of the renal pelvis and ureter. (5) Finally, the urgency of full urological investigation, including excretion pyelography in cases of hæmaturia, is well demonstrated.

Pulmonary Eosinophilia and Staphylococcal Infection.—G. W. Scott, M.D., M.R.C.P. (for Leo Gilchrist, M.D., M.R.C.P.).

R. T., aged 29, had been a known asthmatic since he was 18 months old. Asthmatic attacks had been severe and prolonged during the past year. A two-week course of prednisolone was given with good effect in October 1957 and again in December 1957. In January 1958 a course of desensitization injections was stopped as it produced an attack of asthma. Three years ago he had struck his head against the Leaning Tower of Pisa causing a scalp infection and since then he had recurrent boils. Two weeks before admission, a severe attack of asthma started with productive cough, night sweats and fever. Sputum culture grew coagulase-positive *Staph. aureus* but antibiotic treatment at home was ineffective.

On admission (April 1958).—He was seriously ill and toxic, with temperature 102° F., tachycardia and persistent asthma. Chest radiograph showed patchy opacities in both lungs, most marked in the mid-zones, where it was confluent (Fig. 1). The blood count showed a striking eosinophilia, namely, 67% (24,090 per c.mm.) of a total leucocyte count of 37,000 per c.mm. The sputum contained pus cells and a few eosinophils and there was a good growth of *Staph. aureus*. There was a moderate growth of monilia in two specimens but no other fungi were found. He was treated with Terramycin and Nystatin but his condition deteriorated and on the ninth day after admission he was semi-comatose and *in extremis* with status asthmaticus. Sensitivity tests showed the *Staph. aureus* to be insensitive to Terramycin. Treatment was changed to chloramphenicol 500 mg. six-hourly. He was also given 300 mg. of intravenous hydrocortisone during the next twelve hours followed by oral prednisone 10 mg. six-hourly. The bronchospasm cleared within two days and after a week the eosinophils fell to 3% (420 per c.mm.) of a leucocyte count of 14,000 per c.mm. There was striking improvement in the chest radiograph within a week, but it took five weeks for the shadowing in the left lung to clear, leaving a residual area of atelectasis in the right upper lobe (Fig. 2). *Staph. aureus* was still obtained

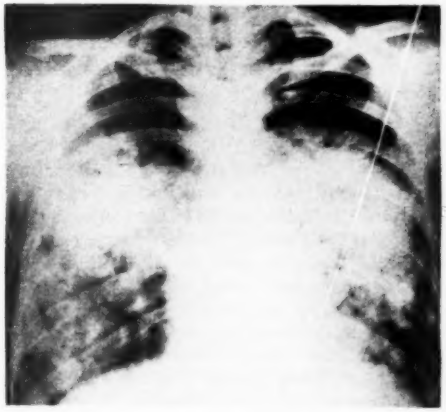

Fig. 1.—Chest radiograph on admission showing patchy opacities in both lungs, most marked in the mid-zones where it was confluent.

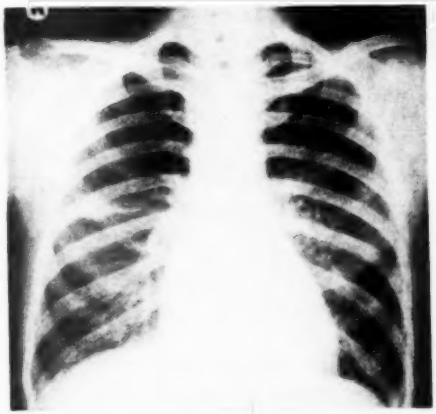

Fig. 2.—Chest radiograph five weeks after starting steroid therapy.

from the sputum up to four weeks after starting chloramphenicol, but subsequent cultures were negative. Antibiotic treatment lasted for six weeks and the patient is still on a maintenance dose of prednisone as an out-patient. He has remained well apart from minor attacks of wheezing.

During his first week in hospital he developed a pustular rash on the face, chest and arms. The pustules later changed into raised, reddish-brown granulomatous lesions, and some of these became hæmorrhagic and necrotic. The patient was found to be taking syrupus caffeine iodide which he had been taking intermittently for some months and which he had brought into hospital. The lesions were regarded as typical iodide granulomata. The iodides were stopped and the rash cleared within a week while on steroid therapy.

Conclusion.—This patient had severe pulmonary eosinophilia with asthma, and the finding of *Staph. aureus* repeatedly in the sputum suggested that infection with this organism was either a precipitating or an exacerbating factor. There was a dramatic response to treatment with prednisone and appropriate antibiotics. As pointed out by Rose and Spencer (1957) it may be impossible, on clinical grounds, to distinguish the respiratory phase of polyarteritis nodosa from the more severe cases of pulmonary eosinophilia as described by Crofton *et al.* (1952). This patient may ultimately develop a generalized polyarteritis, but there have been no signs of this up to nine months after his original illness.

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Intestinal Lipodystrophy (Whipple's Disease).—H. ECONOMIDES, M.B. (for S. KARANI, M.R.C.P.).

Mr. F. P., aged 40.

Admitted 6.3.58 complaining of pale bulky stools four times daily, anorexia and lassitude for five months, whiteness and numbness of hands when cold for four months, bilateral ankle swelling for one month. Weight loss 2 st. in five months.

Past history.—September 1957, while working with high explosive powders, scaling red rash on face, hands, feet, ankles. Occupation changed, rash cleared in eight weeks. No cough or joint pains.

On examination.—Lid lag present. No evidence of thyrotoxicosis. Blood pressure 130/80. Bilateral pitting ankle œdema. Abdomen distended, no organs or masses palpable. No ascites. Small lymph nodes both axillæ.

Investigations.—Hb 83%, M.C.H.C. 28%, W.B.C. 6,000, normal differential. E.S.R. 41 mm. in one hour. Film: some macrocytes, some hypochromic (Wintrobe). Sternal marrow: Hypercellular, partial normoblastic, partial megaloblastic red cell development.

Stools: Occult blood positive, tryptic activity present. Fat absorption test 87%, 84%, 77% absorption. Plasma proteins: Total 4.6, albumin 2.3, globulin 2.3 grams/100 ml. Electrophoresis, decrease in albumin, slight increase in diffuse gamma globulin. Serum Ca 8.8, inorganic phosphorus 4.1 mg./100 ml., alkaline phosphatase 14 K.A. units.

Histamine test meal: Free acid present. Glucose tolerance test: flat curve. Water load: impaired excretion. Vitamin-A-absorption test: Plasma resting level 195 i.u./100 ml.; four hours after 350,000 i.u. vitamin A (oral) 710 i.u./100 ml. Urinary calcium 55 mg./twenty-four hours.

X-rays: Barium meal, no significant abnormality. Abbreviated skeleton, early to moderate osteoporosis thin cortical bone type.

Laparotomy (Mr. F. Graves) 28.4.58.—Lumen slightly larger, wall thicker than normal in proximal two-thirds small bowel. Lacteals of bowel and mesentery distended, mesenteric lymph glands enlarged. Liver and spleen normal.

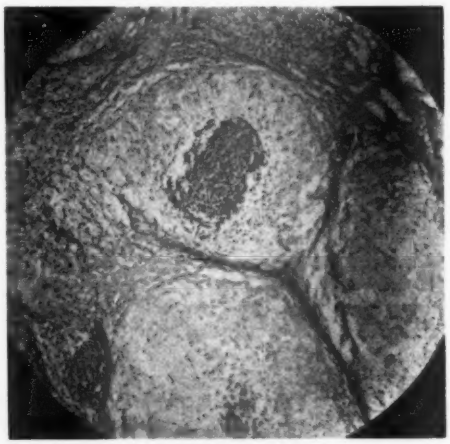

FIG. 1.—Section of lymph node showing foamy macrophages. × 55.

TABLE I.—TREATMENT, CLINICAL PICTURE AND INVESTIGATIONS

	Duration and clinical picture	Investigations
Prednisone 40 mg. daily + folic acid	12 days from 20.6.58 Gradual weight increase Normal stool daily	(1) Vitamin A absorption test: Fasting level 175 i.u./100 ml. 4 hr. after 350,000 i.u. 1,450i.u./100 ml. (2) Urinary Ca 164 mg./24 hr.
Prednisone 20 mg. daily + folic acid	50 days Weight increasing Signs corticosteroid over-dosage Joint pains. Left knee effusion B.P. 140/90	(1) Plasma proteins: Total 7·3, albumin 3·9, globulin 3·4 gram/100 ml. (2) Serum Ca 9·3 mg./100 ml. (3) Serum electrolytes normal (4) Hb 81%
Triamcinolone 16 mg. daily + iron + folic acid	21.8.58 till 12.2.59 Weight steady. Symptom free apart from aching in ankles. Right knee effusion after 42 days—now gone Normal stool daily B.P. 120/80	(1) Plasma proteins: Total 7·2, albumin 4·1, globulin 3·1 grams/100 ml. (2) Serum Ca 10 mg./100 ml. (3) Hb 103%
Triamcinolone 8 mg. daily + iron + folic acid	29 days symptom-free apart from aching in ankles	Investigations within normal limits

Section of lymph node (ileal mesentery): Structure replaced by follicular arrangement of fat-filled cells with fibrous tissue between. Node would appear to drain small intestine, seat of lipodystrophy (Dr. I. G. Williams) (Fig. 1).

The diagnosis of intestinal lipodystrophy was established and treatment with folic acid and prednisone given. Prednisone had a beneficial effect (Table I). Signs of corticosteroid over-dosage in August, treatment changed to triamcinolone. The patient is now symptom free apart from aching in ankles.

Discussion.—Whipple (1907) was the first to recognize this condition when he described the case of a 36-year-old physician who died following five and a half years' polyarthritis, four months' steatorrhœa, gradual weight loss and anæmia. He proposed the name intestinal lipodystrophy because the disease was characterized anatomically by deposits of fat and fatty acids in the intestinal and mesenteric lymphatic tissue. The predominant cell was the foamy macrophage. In 1949 Black-Schaffer, following up Whipple's original observation that not all the macrophages took up fat stains, identified the intracellular inclusion as a polysaccharide. The source of this material has not been determined as yet. Farnan (1958) suggests that intermittent systemic dissemination may account for the widespread lesions found and excessive formation may cause obstruction at the mucosal site. This would account for the steatorrhœa and malabsorption defects.

The features common to most cases described are arthritis, usually preceding steatorrhœa, weight loss, emaciation, pigmentation, achlorhydria and flat glucose tolerance curves. The present case differs in that the arthritis succeeded the steatorrhœa, free acid was present in the gastric juice and the anæmia was megaloblastic.

Treatment.—The course used to be invariably fatal, usually within five years. In 1953 Jones *et al.* published the case report of a patient who following cortisone therapy had a remission for the twelve months she was followed up. Other reports favoured the use of hydrocortisone.

Our patient was treated with prednisone and subsequently triamcinolone with encouraging results.

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Facial Apraxia.[1]—D. A. F. MCGILL, M.D., M.R.C.P. (for E. R. BOLAND, C.B.E., M.D., F.R.C.P.).

H. M., male, aged 52. In November 1950 he developed an infective thrombophlebitis following an injury to his leg. Then followed three episodes of pulmonary infarction and, one month after admission, he developed a left-sided hemiplegia and a facial weakness. One week later he developed a thrombosis of the common iliac veins and he was discharged after three months with a residual paresis. He remained well until June 1957, when there was the sudden onset of inability to speak, move his jaw or his tongue. At this time he felt dizzy and nauseated; he was treated by his general practitioner and recovered in approximately one week. In October 1958, whilst standing on a station

[1]This case was also shown, by Dr. Ian Mackenzie, at a meeting of the Section of Neurology at the National Hospital for Nervous Diseases, on December 4, 1958.

platform, once again there was the sudden onset of inability to speak, move his jaw or his tongue; he developed a severe occipital headache, vomited several times and developed an odd emotional change, alternately crying and laughing. He was not incontinent of urine or fæces and was able to walk with difficulty.

On examination.—Normotensive, blood pressure 150/85. He was orientated in space and in time, had normal intelligence and memory but could too easily be made to laugh and cry. He could understand the written and the spoken word but he could not speak. He could not close his eyes, move his face, open his mouth or protrude his tongue to order but he could blink, laugh, close his eyes to sleep, yawn and cough. He was unable to swallow food but he did swallow saliva unconsciously. He found it easier to write with his left hand although normally right handed and he tried to smoke cigarettes through his nose. There was slight weakness of the right hand, no significant change in the deep reflexes but the plantar responses were extensor.

Over the period of eight weeks there was a slow recovery and on discharge he could close his eyes, open his mouth and swallow soft foods.

Comment.—The physical signs are those of an apraxia involving the muscles of the face, jaw, tongue, pharynx and larynx, together with an apraxia of the right hand. With this apraxia is evidence of a bilateral upper motor neuron lesion with possibly an associated pseudo-bulbar palsy. It is possible to explain the facial apraxia on one lesion and this probably cortical, affecting the lower part of the pre- and post-central gyrus on the left side (Nathan, 1947) but in this particular patient it is felt that there must be two lesions, one in each hemisphere. The lesions are probably vascular; possibly the initial episode was embolic and the more recent one thrombotic in nature.

REFERENCE

NATHAN, P. W. (1947) *Brain*, **70**, 449.

The following cases were also shown:

Pyrexia of Unknown Origin with Eosinophilia, ? Splenomegaly and Bilateral Renal Opacities.—Dr. H. R. OVERY (for Dr. RICHARD ASHER).

This man, who was too ill to come to the meeting, died soon afterwards. The post-mortem showed a disseminated anaplastic malignant process of uncertain origin, accounting for the quasi-splenomegaly and eosinophilia. The renal opacities apparently were due to exogenous material so far not identified.

Carcinoma of the Lung with Nephrotic Syndrome. ? Renal Vein Thrombosis.—Dr. A. J. LEVI (for Miss MURIEL WATERFALL).

Steatorrhœa with Megaloblastic Anæmia.—Dr. J. PEARCE (for Dr. F. A. ELLIOTT).

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BOOK REVIEWS

Staphylococcus pyogenes and its Relation to Disease. By Stephen D. Elek, M.D., D.Sc., Ph.D., D.P.H. (Pp. vii+767; illustrated. 84s.) Edinburgh and London: E. & S. Livingstone Ltd. 1959.

It is inconceivable that another edition of "Kolle and Wassermann" or the Medical Research Council "System of Bacteriology" will ever be published: the subject has grown too large. The full encyclopædic treatment is now only possible for a single genus or even species, and it is about one species that Professor Elek has written this large book, which concludes with a bibliography occupying 188 pages. It is perhaps for this stupendous compilation of references that the book will be most valued: anyone seeking information on an obscure point will not only find it dealt with in the text, but can then refer to original sources. From an interesting historical survey, the author proceeds to consider morphology, metabolism, ecology, the formation of toxins and other products, the difficult problems of virulence and immunity, susceptibility to physical and chemical agents and to antibiotics, and finally clinical problems of staphylococcal infection, with special reference to the kind of hospital infection which is now so complex and serious a problem. In the efforts in which so many are now engaged to tackle a form of infection which seems to defy control, whether hygienic or along the paths of immunization or chemotherapy, study of this book may suggest new lines of approach, or—perhaps more probably—save the reader wasted effort by informing him that his bright original idea was exploited and found wanting by someone else years ago. There are many excellent illustrations: some of their legends (e.g. those of Figs. 7, 8 and 40) are not sufficiently explanatory. The only criticism that might be offered of the text as a whole is that the author too often withholds his own judgment on disputed questions. Every enterprising bacteriologist should have facilities for consulting this monumental work.

Practical Blood Grouping. By F. Stratton, M.D., D.Sc., D.P.H., and P. H. Renton, M.D., B.Sc. (Pp. xxiv+331; illustrated. 42s.) Oxford: Blackwell Scientific Publications. 1958.

This is essentially a practical manual on blood grouping for those engaged in such work, but it also covers in a sensible way some of the theory behind the procedures. The book begins with a useful chapter, which is not too elaborate, on antigens and antibodies in general, and then proceeds to a description of the various methods used in agglutination tests. Other chapters cover the causes of false results in agglutination tests (a very valuable chapter), the antiglobulin test, the identification of atypical antibodies, and the individual blood-group antigens which are discussed in reasonable detail. A chapter on the organisation of large-scale blood grouping is a useful inclusion. Many of the chapters are made much more easy to follow than would be expected by the addition of appropriate case histories which serve as practical examples of many problems; there are also some good illustrations. This book should prove excellent value for those involved in routine blood grouping, and a valuable source of references on the subject.

Coffee and Caffeine. By Dr. Med. Rolf Ulrich. Translated by Janet Ellingham. (Pp. 52; 7s. 6d.) Bristol: John Wright & Sons Ltd. 1958.

The author paints the case against coffee and caffeine in gloomy colours. Despite the heavy consumption of such drinks really valid evidence is not so very large. Nevertheless one is relieved to find that they constitute a smaller evil than either nicotine or alcohol. Most of the references are to pre-war work but he draws attention to the paucity of our knowledge of the real effects of the caffeine-containing cold soft drinks. The translation is adequate but the case is probably spoiled by over-emphasis.

Lesions of the Lower Bowel. By Raymond J. Jackman, M.D., M.S. (Pp. xxxvii+347; illustrated. £5 17s. 6d.) Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1958.

"Lesions of the Lower Bowel", by R. J. Jackman of the Mayo Clinic, is an attractive book, whose purpose is to convince readers that almost two-thirds of lesions of the entire large intestine occur in the distal part and are easily diagnosed by proctoscopy (sigmoidoscopy) before resorting to an X-ray. Further, sigmoidoscopy gives good evidence of lesions higher in the alimentary tract.

The author has achieved his objective. The book consists of 29 chapters with 333 pages of reading, 56 figures and 75 coloured plates.

The arrangement is unusual being on a clinical rather than a pathological basis, but a wealth of

physical signs, pathological conditions and functional disturbances is dealt with. The emphasis is on diagnosis, with sound but brief indications on treatment. The facts and opinions are based on the analysis of a large number of recent cases seen at the Mayo Clinic. This book should be scanned by the physician and surgeon and then read carefully. The reviewer did so with relish and instruction. Undoubtedly the sigmoidoscope is as indispensable in gastro-enterological conditions as are the stethoscope and the sphygmomanometer in cardiovascular lesions. It should be used more often.

The anatomy chapter is discursive and brief. The musculature of the anal canal, more accurately demarcated by several British surgeons, could, with advantage, have been included. The references are recent and almost exclusively American. Much good material on the subjects dealt with has been steadily published in Britain in the last thirty years.

The black and white illustrations are good, the 75 coloured plates are very good, and warrant purchase of the book. They merit an occasional review to refresh the memory of possibilities.

The extra-rectal conditions, although admittedly rare, are surprising in their variety.

This book is a "must" for the bookshelf of every general surgeon and physician.

Industrial Health Technology. By Bryan Harvey, M.A., M.Sc., Assoc.I.Mech. E., and Robert Murray, B.Sc., M.B., Ch.B., D.P.H., D.I.H. (Pp. xiii+337; illustrated. 45s.) London: Butterworth & Co. (Publishers) Ltd. 1958.

The authors of this brilliant book, a doctor and an engineer, are as they say, Jacks-of-all-trades, and in this age of over-specialization, it is all the better for that. The study of the health and diseases of the industrial worker is primarily the concern of doctors, though the application of preventive measures is largely in the hands of engineers, chemists and physicists. Close co-operation between doctors and engineers and other technologists is needed in the fight against occupational disease, but it is also essential that both groups should have wide practical experience of the working conditions and the personal relationships found in industry. As members of the Factory Department, the authors have had this practical experience in full measure, and they have clearly kept their eyes and ears open in going about their work. In combining the distillations of their experience and observations, they have produced a book of outstanding usefulness.

The title "Industrial Health Technology" does not cover the scope of the book. The word "technology" in this sense means the application of engineering, chemical and physical techniques to the study of industrial environments. Nearly half the book is devoted to giving sound and simple information about industrial diseases and poisoning as well as industrial psychology and physiology. It has been written mainly for industrial executives and trade-unionists, because they are more closely concerned with the running of factories and with the day-to-day application of preventive measures against occupational health risks.

The book, which is written in a simple and entertaining prose style, is divided into three parts. The first and longest deals with the causes of industrial disease. The second describes and classifies preventive measures and includes a notable chapter on the principles and practice of exhaust ventilation. In the third part there is an excellent discussion of the factors which contribute to the comfort or discomfort of the worker, such as ventilation and heating, lighting, colour and noise. The importance of morale and good personal relationships is stressed. The legal requirements of the Factories Acts and regulations applying to various processes are given under the appropriate headings, and the provisions of the Industrial Injuries Act, concerning industrial diseases, are given in detail.

It is the judicious mixture of the historical and wider view with closely organized medical, technical and legal information which makes the book so attractive and useful. It is well produced and illustrated and the proof reading has been carefully done.

Handbook of Respiration. Compiled by Philip L. Altman, John F. Gibson, Jr., M.D., Charles C. Wang. Edited by Dorothy S. Dittmer and Rudolph M. Grebe. (Pp. xv+403; 52s. 6d.) Philadelphia and London: W. B. Saunders Company, Ltd. 1958.

This book will be of interest not only to the medical man but also to the biologist as it is written to cover a large field and one would have to refer widely to other sources to discover the information it contains on the physical, chemical, biological and medical aspects of respiration. As this would suggest, a large part of the book is only of passing interest to the medical man, but despite the fact that it is composed entirely of tables and nomograms, it is an interesting book to read.

Most of it concerns the normal subject and the alterations brought about by exercise, pressure change, inhaled gases and drugs. The references following each subject are in most cases very adequate and enhance the value of the book.

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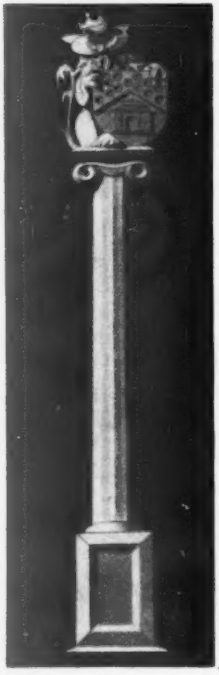

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